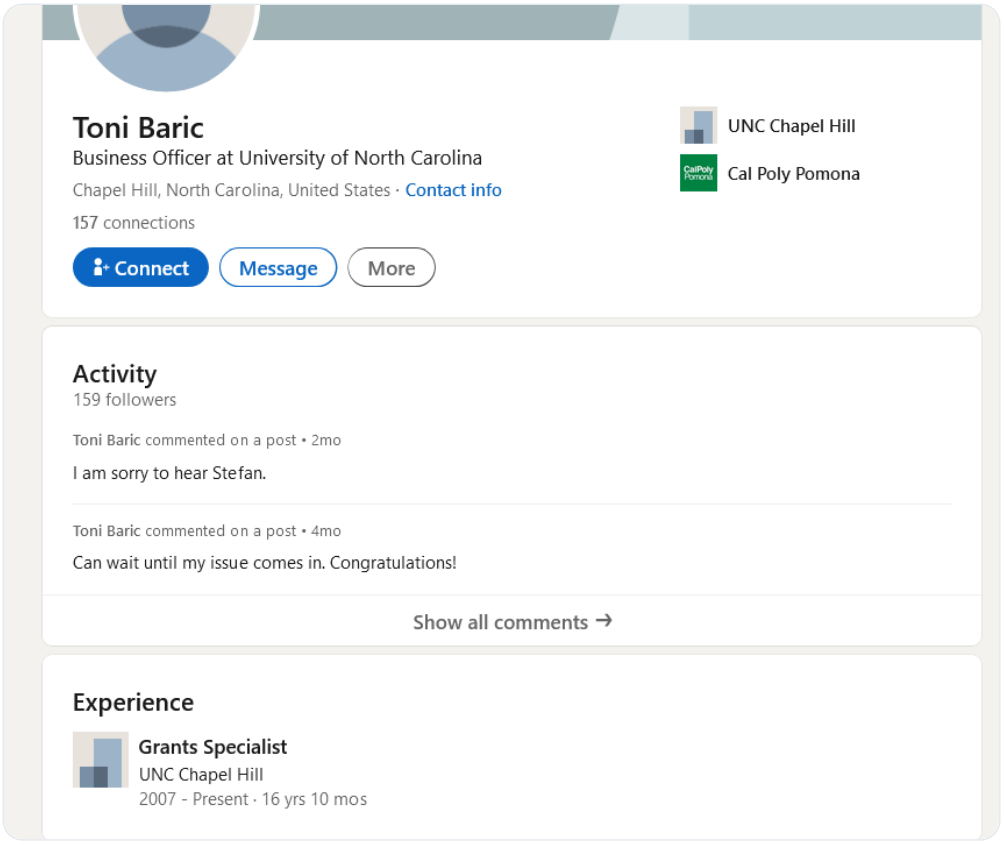
Destiny Rezendes @dezzie_rezzie

Oct 25, 2023 · 13 tweets · dezzie_rezzie/status/1716984766342279480

🧵1🔍 Who is Ralph Baric, really? We all know that he's the world's expert on coronaviruses & he is implicated in the lab leak 'theory' that resulted in the C19 pandemic, but do you REALLY know Baric & how important his role in C19 is?

2🧵In previous threads I have extensively looked into the career of Ralph Baric. Along the way I discovered that Baric's wife, Antoinette 'Toni' also works at UNC Chapel Hill as the school's Grant Specialist. Convenient.



3🧵When looking into this months ago I noticed Baric's CV listed his family member, which confirmed Antoinette Baric was indeed Ralph's wife. Also listed were two daughters [Cristina & Michelle], & two son's [Michael & Thomas]

Curriculum Vitae
Ralph S. Baric

I. PERSONAL INFORMATION:

A. Business Address:
Department of Epidemiology
School of Public Health
University of North Carolina at Chapel Hill
McGaveran-Greenberg Hall, CB# 7435
Chapel Hill, North Carolina 27599-7435
Phone: 919-966-3895

Home Address:
2600 Northstream Ct
Haw River, NC 27258
336-578-1575

B. Personal Data
Born: April 3, 1954
US Citizen

Married: Antoinette Baric
Children: Cristina, Michelle, Michael, Thomas

II. EDUCATION:

A. North Carolina State University, Raleigh, North Carolina, B.S., Zoology, 1977
B. North Carolina State University, Raleigh, North Carolina, Ph.D., Microbiology, 1983
C. University of Southern California, School of Medicine, Department of Microbiology and Neurology, Post-doctoral Fellow, 1982-1986

III. PROFESSIONAL EXPERIENCE:

A. Assistant Professor, Department of Parasitology and Laboratory Practice, University of North Carolina at Chapel Hill, March 1986-June 1990
B. Assistant Professor, Department of Epidemiology, University of North Carolina at Chapel Hill, July 1990-June 1993.
C. Associate Professor, Department of Epidemiology, University of North Carolina at Chapel Hill, July 1993-2001.
D. Associate Professor, Department of Microbiology and Immunology, University of North Carolina at Chapel Hill, July 1993-2001
E. Professor, Department of Epidemiology, Department of Microbiology and Immunology, University of North Carolina at Chapel Hill, July 2001-current

4🧵 In December of 2021, the NC regional Pulitzer-prize winning newspaper wrote a glowing article about Ralph Baric, announcing that he had just been given the highest civilian honor in the state by the governor. The article mentioned almost all aspects of Baric's life-almost..

Link: https://archive.ph/DQreQ

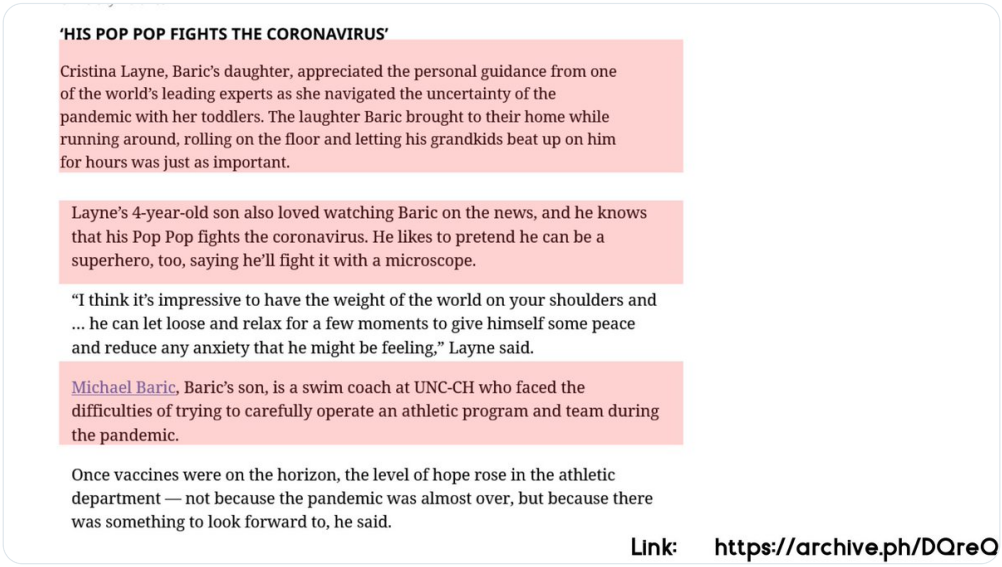
For his contributions to the development of the Moderna vaccine as well as Remdesivir and Molnupiravir, which are COVID-19 drug treatments, Baric is The News & Observer's 2021 Tar Heel of the Year. The distinction honors North Carolina residents who have made significant contributions to the state and region — and in this case, the world.

Dr. Ralph Baric, a scientist at UNC-Chapel Hill's Gillings School of Global Public Health, has studied coronaviruses for decades. Baric and researchers in his lab helped develop the Moderna vaccine and treatments for COVID-19 like Remdesevir. BY JULIA WALL

A COMMITMENT TO THE PROCESS

Baric's research was the basis for multiple vaccines, including Moderna, which was tested on animal models in his UNC-CH lab before it was given to people. His team also conducted the pre-clinical development for the only approved direct-acting antiviral drug, Remdesivir, to treat COVID-19 patients in hospitals. Baric's lab also studied Molnupiravir, which is the first antiviral pill shown to treat COVID-19 and was authorized for emergency use last month.

Link: https://archive.ph/DQreQ



'HIS POP POP FIGHTS THE CORONAVIRUS'

Cristina Layne, Baric's daughter, appreciated the personal guidance from one of the world's leading experts as she navigated the uncertainty of the pandemic with her toddlers. The laughter Baric brought to their home while running around, rolling on the floor and letting his grandkids beat up on him for hours was just as important.

Layne's 4-year-old son also loved watching Baric on the news, and he knows that his Pop Pop fights the coronavirus. He likes to pretend he can be a superhero, too, saying he'll fight it with a microscope.

"I think it's impressive to have the weight of the world on your shoulders and ... he can let loose and relax for a few moments to give himself some peace and reduce any anxiety that he might be feeling," Layne said.

Michael Baric, Baric's son, is a swim coach at UNC-CH who faced the difficulties of trying to carefully operate an athletic program and team during the pandemic.

Once vaccines were on the horizon, the level of hope rose in the athletic department — not because the pandemic was almost over, but because there was something to look forward to, he said.

Link: https://archive.ph/DQreQ

"It made me very proud, because I know he played a huge role in that," Michael Baric said.

For Toni, her husband brought a sense of relief during the pandemic and pride as she collected messages of gratitude from others.

One email came from a UNC-CH faculty member whose sister recovered from COVID-19 after being treated with Remdesevir. Another email was sent by a mom who thanked Baric for saving her son's life.

"The state and the country and the world are really lucky that Ralph did that, starting decades ago," said Johnston, a professor emeritus of microbiology and immunology at the UNC School of Medicine and the executive director of the nonprofit organization Global Vaccines Inc.

Link: https://archive.ph/DQreQ

5🧵 The article mentions his wife, Toni, their long history at UNC, their son, Michael who also works at UNC as a swim coach, their daughter, Cristina & even Baric's grandkids. No mention tho of Michelle & Thomas Baric. The other children...

In 2015, Baric and his colleagues at UNC-CH started working on Remdesevir, without knowing that in a few years it would be saving lives of patients at the hospital across the street and at those around the country. More than half of patients hospitalized with COVID-19 are given Remdesevir, according to biopharmaceutical company Gilead Sciences.

About two to three years before the COVID-19 pandemic, Baric and his colleagues started testing mRNA-based vaccines against other coronaviruses. The mRNA vaccines essentially teach cells how to make a protein that triggers an immune response that attacks the virus. Scientists like Baric have been pioneering that technology since the 1990s.

Their data was "spectacular" in animal models of human disease in how it could neutralize the virus through immune responses and protect young and old animals from lethal disease, Baric said. That data was rolling out just as SARS CoV-2 emerged, so Baric and other scientists used it as the foundation to develop vaccines to fight COVID-19.

Link: https://archive.ph/DQreQ

In collaboration with the NIH, Baric's lab was charged with developing similar animal models to test vaccine candidates by April 2020 and gather data by the end of June 2020, so it could be sent to the FDA to get approval for Phase 3 testing in humans, which began in August 2020.

"That trusting relationship and their expertise in animal model development allowed for early understanding of how efficacious COVID-19 vaccines were and undoubtedly led to the record speed of development," Corbett said.

She is an assistant professor of immunology and infectious diseases at Harvard University who worked with Baric while earning her doctorate at UNC-CH. Corbett helped develop the Moderna vaccine as a research fellow at the National Institute of Allergy and Infectious Diseases' Vaccine Research Center.

Graham, former deputy director of the NIAID Research Center at NIH, called Baric "the premier coronavirologist in the world.

Link: https://archive.ph/DQreQ

PREPARING FOR THE NEXT OUTBREAK

While Baric and his team have hit remarkable milestones throughout the pandemic, the celebratory moments have been fleeting.

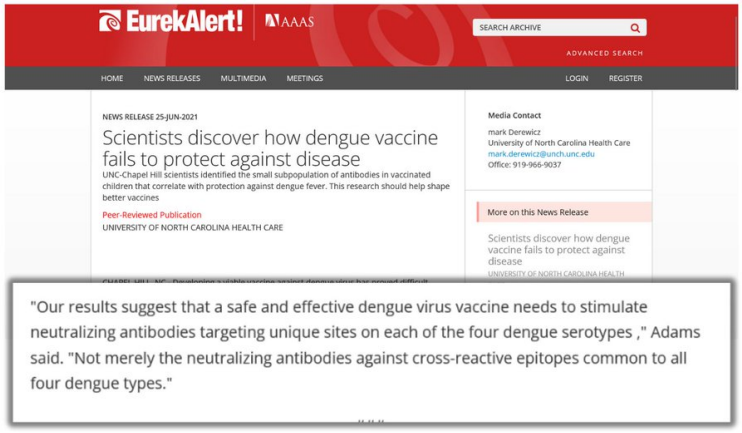
The day before a U.S. Food and Drug Administration panel gave preliminary approval to Molnupiravir in November, the omicron variant emerged. Baric's lab geared up to respond to that variant to understand its biology, its impact on therapeutics, vaccines and drugs, and how best to counter it if some of the products that are on a shelf lose their potency, Baric explained.

Accomplishments: Inducted into the National Academy of Sciences in 2021; UNC System O. Max Gardner Award in 2021; North Carolina Award in 2020.

Fun fact: Before the pandemic, Baric and his wife would eat lunch together nearly every day at UNC-Chapel Hill. Sometimes they would invite their son, Michael, who also works at UNC.

Link: https://archive.ph/DQreQ

6🧵 I found this very odd. Not only was Thomas Baric missing from the article, but also from Baric's CV. It took some digging but lo' & behold, Thomas Baric ALSO works at UNC, in fact he's on his way to follow his dad's footsteps; working on viruses/vaccines!



Link: https://www.eurekalert.org/news-releases/903503

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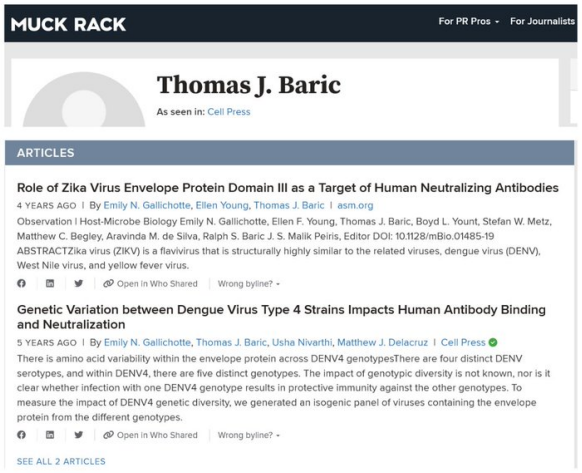
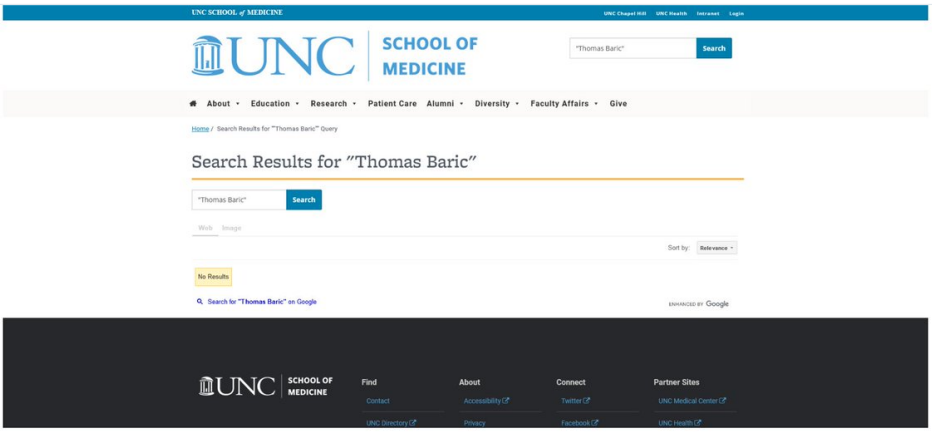


Link: https://muckrack.com/thomas-j-baric

Link: https://reporter.nih.gov/search/0vwNTqyItkC2pzco-LJNSA/project-details/9153244

7🧵Thomas Baric is listed as a scientist and co-author of multiple papers with his father Ralph working on the same studies that Ralph had been working on leading up to the pandemic including federally funded work. However, you don't find him if you search UNC's website. 🤔



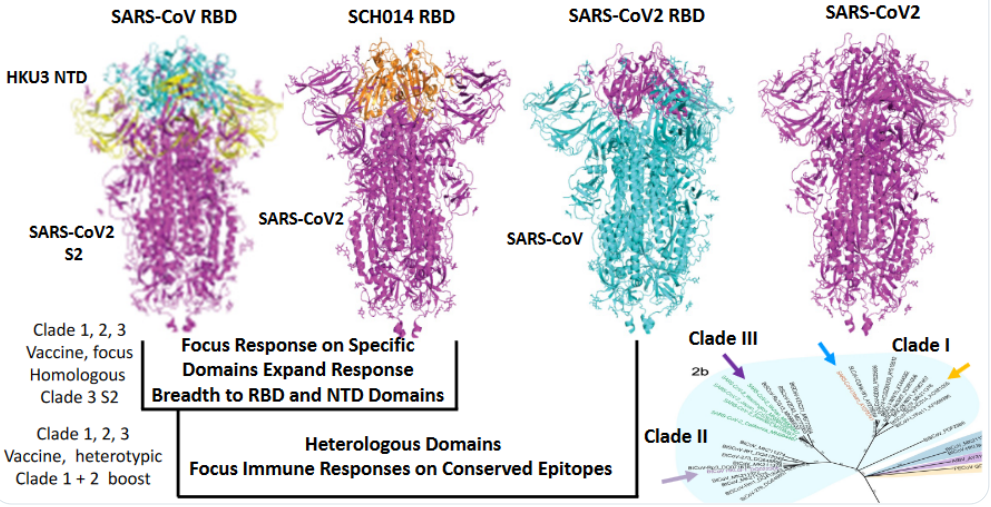
Link: https://www.med.unc.edu/?s=%22Thomas+Baric%22&cx=017059784719810698204%3Alj2ibo0i4wo&cof=FORID%3A10&ie=UTF-8&search-btn=Search&search_type=gcs#gsc.tab=0&gsc.q=%22Thomas%20Baric%22&gsc.page=1

8🧵I only found out due to a March 2022 WHO consultation document by UNC Chapel Hill titled, Major challenges w/the development of Pan-Coronavirus Vaccines, where on the last page is listed "Tommy Baric" & Acknowledged is Pfizer, Merck, Zuckerberg, & NIAID.

Common Obstacles

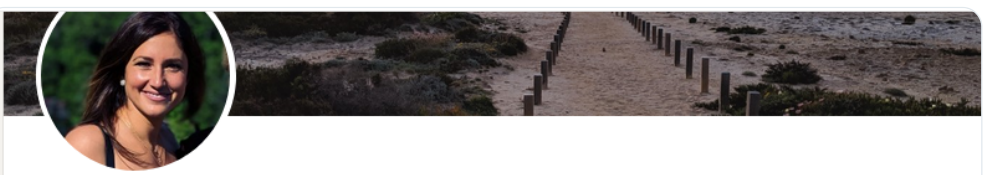
- **Sarbecoviruses**
  - Group II and Group III strains and assays
  - More High Risk Strains
- **Other Betacoronaviruses-**
  - MERS-CoV (group 2c)
    - heterologous group 2c high-risk strains/models
  - Group 2d strains (to be identified and developed)
  - Group 2a (HCoV OC43/HKU1)
    - limited reagents/animal models
    - lots of animal strains (surrogates)
- **Other Alphacoronaviruses**
  - NL63 and HCoV229E animal models (weak/nonexistent)
  - High Priority Zoonotic Strains (to be identified and developed)
    - Several animal strains/models available
- **Deltacoronaviruses**
  - Porcine epidemic diarrhea virus
  - Other high priority strains (to be identified and developed)

Chimeric Sarbecovirus Spike Vaccines



9🧵 Seems like Thomas wasn't forgotten from the article of his father's success. He was intentionally not mentioned. The big question is why? But the curiosity doesn't end there. Why nothing more than a mention of Michelle Baric?

10.🧵 Maybe it has something to do with the fact that Michelle works at Myriad Genetics [MG] Why is this relevant. Baric wasn't alone in his honors by the state of NC, another recipient was NIH director Francis Collins, another NC native.



Michelle Baric

Genetic Counselor at Myriad Genetics

Wrightsville Beach, North Carolina, United States · Contact info

185 connections

Connect | Message | More

Myriad Genetics

University of Cincinnati

Activity

184 followers

Michelle hasn't posted yet

Recent posts Michelle shares will be displayed here.

Show all activity →

Experience

Genetic Counselor

Myriad Genetics · Full-time

Aug 2020 - Present · 3 yrs 3 mos

Patient Education Team

Genetic Counselor

Duke University Health System · Full-time

Nov 2015 - Jul 2020 · 4 yrs 9 mos

Durham, NC

Francis Collins

31 languages

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From Wikipedia, the free encyclopedia

For other people named Francis Collins, see Francis Collins (disambiguation).

Francis Sellers Collins ForMemRS (born April 14, 1950) is an American physician-geneticist who discovered the genes associated with a number of diseases and led the Human Genome Project. He served as director of the National Institutes of Health (NIH) in Bethesda, Maryland, from 17 August 2009 to 19 December 2021, serving under three presidents.[1][2]

Before being appointed director of the NIH, Collins led the Human Genome Project and other genomics research initiatives as director of the National Human Genome Research Institute (NHGRI), one of the 27 institutes and centers at NIH. Before joining NHGRI, he earned a reputation as a gene hunter at the University of Michigan.[3] He has been elected to the Institute of Medicine and the National Academy of Sciences, and has received the Presidential Medal of Freedom and the National Medal of Science.

Collins also has written books on science, medicine, and religion, including the *New York Times* bestseller, *The Language of God: A Scientist Presents Evidence for Belief*. After leaving the directorship of NHGRI and before becoming director of the NIH, he founded and served as president of The BioLogos Foundation, which promotes discourse on the relationship between science and religion and advocates the perspective that belief in Christianity can be reconciled with acceptance of evolution and science, especially through the idea that the Creator brought about his plan through the processes of evolution.[4] In 2009, Pope Benedict XVI appointed Collins to the Pontifical Academy of Sciences.[5]

On October 5, 2021, Collins announced that he would resign as NIH director by the end of the year.[6] Four months later in February 2022, he joined the Cabinet of Joe Biden as Acting Science Advisor to the President, replacing Eric Lander.[7][8]

Early years [edit]

Collins was born in Staunton, Virginia, the youngest of four sons of Fletcher Collins and Margaret James Collins. Raised on a small farm in Virginia's Shenandoah Valley, Collins was home schooled until the sixth grade.[9] He attended Robert E. Lee High School in Staunton,

Francis Collins

Science Advisor to the President
Acting
In office
February 18, 2022 – October 3, 2022

President	Joe Biden
Preceded by	Eric Lander
Succeeded by	Arati Prabhakar

16th Director of the National Institutes of Health
In office
August 17, 2009 – December 19, 2021

President	Barack Obama Donald Trump Joe Biden
Deputy	Lawrence A. Tabak

Dr. Kizzmekia Corbett speaks to members of the graduating class and parents at the University of North Carolina commencement exercises Friday, May 14, 2021. BY UNC

A group of nine North Carolinians spanning the fields of microbiology and immunology, education, public service, history and fashion received the state's highest civilian honor during a ceremony Thursday evening.

Recipients of the North Carolina Award for 2021 and 2020 (since last year's ceremony was canceled due to the pandemic) include Dr. Francis Collins, the outgoing director of the National Institutes of Health who has led the federal agency for the last 12 years; Dr. Ralph Baric, a renowned coronavirus researcher at UNC-Chapel Hill; and André Leon Talley, who grew up in Durham and went on to work at several fashion publications, including Vogue.

Established by state lawmakers in 1961 and first awarded in 1964, the North Carolina Award recognizes "significant contributions to the state and nation in the fields of fine arts, literature, public service and science," according to the N.C. Department of Cultural and Natural Resources, which administers the award.

More than 250 people have received the award, including Maya Angelou, James Taylor, John Hope Franklin, the Rev. Billy Graham and the Rev. William J. Barber II.

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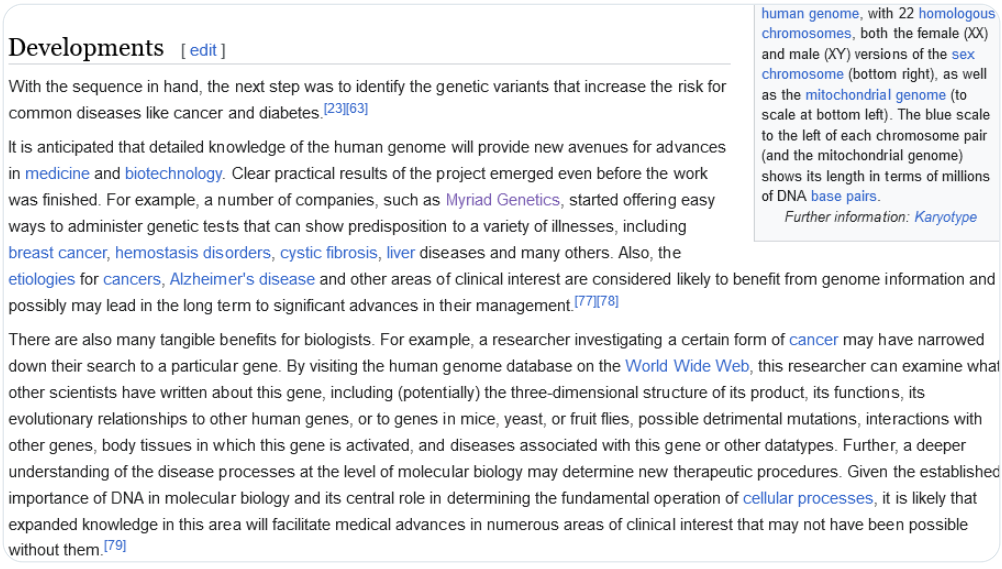
NORTH CAROLINA

Meet the 9 North Carolinians receiving the state's highest civilian honor this year

BY AVI BAJPAI

UPDATED NOVEMBER 19, 2021 10:45 AM

11🧵Here's the kicker, Collins wasn't just Fauci's boss at NIH, he also was the first director of the Human Genome Project at the Nat'l human genome Institute, of which the company leading the sequencing is none other than Myriad Genetics.



human genome, with 22 homologous chromosomes, both the female (*XX*) and male (*XY*) versions of the sex chromosome (bottom right), as well as the mitochondrial genome (to scale at bottom left). The blue scale to the left of each chromosome pair (and the mitochondrial genome) shows its length in terms of millions of DNA base pairs.

Further information: Karyotype

Developments [edit]

With the sequence in hand, the next step was to identify the genetic variants that increase the risk for common diseases like cancer and diabetes.[23][63]

It is anticipated that detailed knowledge of the human genome will provide new avenues for advances in medicine and biotechnology. Clear practical results of the project emerged even before the work was finished. For example, a number of companies, such as Myriad Genetics, started offering easy ways to administer genetic tests that can show predisposition to a variety of illnesses, including breast cancer, hemostasis disorders, cystic fibrosis, liver diseases and many others. Also, the etiologies for cancers, Alzheimer's disease and other areas of clinical interest are considered likely to benefit from genome information and possibly may lead in the long term to significant advances in their management.[77][78]

There are also many tangible benefits for biologists. For example, a researcher investigating a certain form of cancer may have narrowed down their search to a particular gene. By visiting the human genome database on the World Wide Web, this researcher can examine what other scientists have written about this gene, including (potentially) the three-dimensional structure of its product, its functions, its evolutionary relationships to other human genes, or to genes in mice, yeast, or fruit flies, possible detrimental mutations, interactions with other genes, body tissues in which this gene is activated, and diseases associated with this gene or other datatypes. Further, a deeper understanding of the disease processes at the level of molecular biology may determine new therapeutic procedures. Given the established importance of DNA in molecular biology and its central role in determining the fundamental operation of cellular processes, it is likely that expanded knowledge in this area will facilitate medical advances in numerous areas of clinical interest that may not have been possible without them.[79]

	National Institutes of Health
Thesis	*Semiclassical theory of vibrationally inelastic scattering, with application to $H^+ + H_2$* (1974)
Doctoral advisor	James Cross

Several scientific teams worked in the 1970s and 1980s to identify genes and their loci as a cause of cystic fibrosis. Progress was modest until 1985, when Lap-Chee Tsui and colleagues at Toronto's Hospital for Sick Children identified the locus for the gene.[18] It was then determined that a shortcut was needed to speed the process of identification, so Tsui contacted Collins, who agreed to collaborate with the Toronto team and share his chromosome-jumping technique. The gene was identified in June 1989,[19][20] and the results were published in the journal *Science* on September 8, 1989.[21] This identification was followed by other genetic discoveries made by Collins and a variety of collaborators. They included isolation of the genes for Huntington's disease,[22] neurofibromatosis,[23][24] multiple endocrine neoplasia type 1,[25] inv(16) AML[26] and Hutchinson–Gilford progeria syndrome.[27]

Genomics [edit]

In 1993 National Institutes of Health Director Bernadine Healy appointed Collins to succeed James D. Watson as director of the National Center for Human Genome Research, which became National Human Genome Research Institute (NHGRI) in 1997. As director he oversaw the International Human Genome Sequencing Consortium,[28] which was the group that successfully carried out the Human Genome Project.[29]

In 1994 Collins founded NHGRI's Division of Intramural Research,[30] a collection of investigator-directed laboratories that conduct genome research on the NIH campus.[*citation needed*]

In June 2000 Collins was joined by President Bill Clinton and biologist Craig Venter in making the announcement of a working draft of the human genome.[31] He stated that "It is humbling for me, and awe-inspiring to realize that we have caught the first glimpse of our own instruction book, previously known only to God."[32][33][34] An initial analysis was published in February 2001, and scientists worked toward finishing the reference version of the human genome sequence by 2003, coinciding with the 50th anniversary of James D. Watson and Francis Crick's publication of the structure of DNA.[*citation needed*]

Another major activity at NHGRI during his tenure as director was the creation of the haplotype map of the human genome. This International HapMap Project produced a catalog of human genetic variations—called single-nucleotide polymorphisms—which is now being used to discover variants correlated with disease risk. Among the labs engaged in that effort is Collins' own lab at NHGRI, which has sought to identify and understand the genetic variations that influence the risk of developing type 2 diabetes.[*citation needed*]

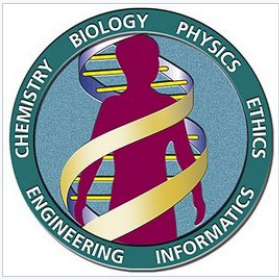
In addition to his basic genetic research and scientific leadership, Collins is known for his close attention to ethical and legal issues in genetics. He has been a strong advocate for protecting the privacy of genetic information and has served as a national leader in securing the passage of the federal Genetic Information and Nondiscrimination Act, which prohibits gene-based discrimination in employment and health insurance.[35] In 2013, spurred by concerns over the publication of the genome of the widely used HeLa cell line derived from the late Henrietta Lacks, Collins and other NIH leaders worked with the Lacks family to reach an agreement to protect their privacy, while giving researchers controlled access to the genomic data.[36]

Building on his own experiences as a physician volunteer in a rural missionary hospital in Nigeria,[37] Collins is also very interested in

Human Genome Project

From Wikipedia, the free encyclopedia

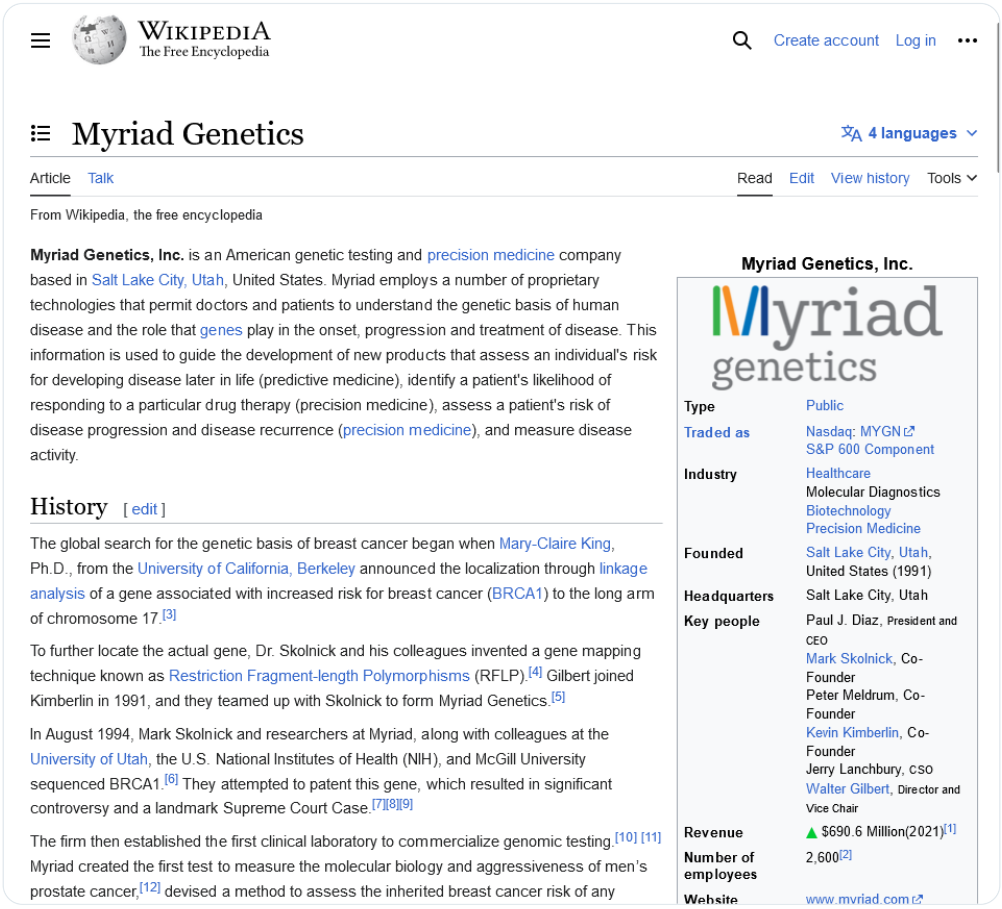
The **Human Genome Project** (**HGP**) was an international scientific research project with the goal of determining the base pairs that make up human DNA, and of identifying, mapping and sequencing all of the genes of the human genome from both a physical and a functional standpoint. It started in 1990 and was completed in 2003.[1] It remains the world's largest collaborative biological project.[2] Planning for the project started after it was adopted in 1984 by the US government, and it officially launched in 1990. It was declared complete on April 14, 2003, and included about 92% of the genome.[3] Level "complete genome" was achieved in May 2021, with a remaining only 0.3% bases covered by potential issues.[4][5] The final gapless assembly was finished in January 2022.[6]



Logo of the Human Genome Project

Funding came from the United States government through the National Institutes of Health (NIH) as well as numerous other groups from around the world. A parallel project was conducted outside the government by the Celera Corporation, or Celera Genomics, which was formally launched in 1998. Most of the government-sponsored sequencing was performed in twenty universities and research centres in the United States, the United Kingdom, Japan, France, Germany, and China,[7] working in the International Human Genome Sequencing Consortium (IHGSC).

The Human Genome Project originally aimed to map the complete set of nucleotides contained in a human haploid reference genome, of which there are more than three billion. The "genome" of any given individual is unique; mapping the "human genome" involved sequencing samples collected from a small number of individuals



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The Free Encyclopedia

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Myriad Genetics

4 languages

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From Wikipedia, the free encyclopedia

Myriad Genetics, Inc. is an American genetic testing and precision medicine company based in Salt Lake City, Utah, United States. Myriad employs a number of proprietary technologies that permit doctors and patients to understand the genetic basis of human disease and the role that genes play in the onset, progression and treatment of disease. This information is used to guide the development of new products that assess an individual's risk for developing disease later in life (predictive medicine), identify a patient's likelihood of responding to a particular drug therapy (precision medicine), assess a patient's risk of disease progression and disease recurrence (precision medicine), and measure disease activity.

History [edit]

The global search for the genetic basis of breast cancer began when Mary-Claire King, Ph.D., from the University of California, Berkeley announced the localization through linkage analysis of a gene associated with increased risk for breast cancer (BRCA1) to the long arm of chromosome 17.[3]

To further locate the actual gene, Dr. Skolnick and his colleagues invented a gene mapping technique known as Restriction Fragment-length Polymorphisms (RFLP).[4] Gilbert joined Kimberlin in 1991, and they teamed up with Skolnick to form Myriad Genetics.[5]

In August 1994, Mark Skolnick and researchers at Myriad, along with colleagues at the University of Utah, the U.S. National Institutes of Health (NIH), and McGill University sequenced BRCA1.[6] They attempted to patent this gene, which resulted in significant controversy and a landmark Supreme Court Case.[7][8][9]

The firm then established the first clinical laboratory to commercialize genomic testing.[10] [11] Myriad created the first test to measure the molecular biology and aggressiveness of men's prostate cancer,[12] devised a method to assess the inherited breast cancer risk of any

Myriad Genetics, Inc.

Myriad genetics

Type	Public
Traded as	Nasdaq: MYGN S&P 600 Component
Industry	Healthcare Molecular Diagnostics Biotechnology Precision Medicine
Founded	Salt Lake City, Utah, United States (1991)
Headquarters	Salt Lake City, Utah
Key people	Paul J. Diaz, President and CEO Mark Skolnick, Co-Founder Peter Meldrum, Co-Founder Kevin Kimberlin, Co-Founder Jerry Lanchbury, CSO Walter Gilbert, Director and Vice Chair
Revenue	▲ $690.6 Million(2021)[1]
Number of employees	2,600[2]
Website	www.myriad.com

12🧵This is a developing story worth looking into. Til then, receipts as always 🧾
https://cdn.who.int/media/docs/default-source/blue-print/2.-baric_r-d-who-consultation_march-25-2022.pdf

Scientists discover how dengue vaccine fails to protect against disease
Researchers discovered that a small subpopulation of antibodies binding to unique sites on each serotype are linked to protection. The research, published in the Journal of Clinical Investigation, pr…

https://www.eurekalert.org/news-releases/903503

archive.ph/DQreQ
https://sph.unc.edu/wp-content/uploads/sites/112/2016/09/CV_Ralph_Baric.pdf
https://www.linkedin.com/in/michelle-baric-123811a3/

Myriad Genetics - Wikipedia

https://en.wikipedia.org/wiki/Myriad_Genetics

Francis Collins - Wikipedia

https://en.wikipedia.org/wiki/Francis_Collins

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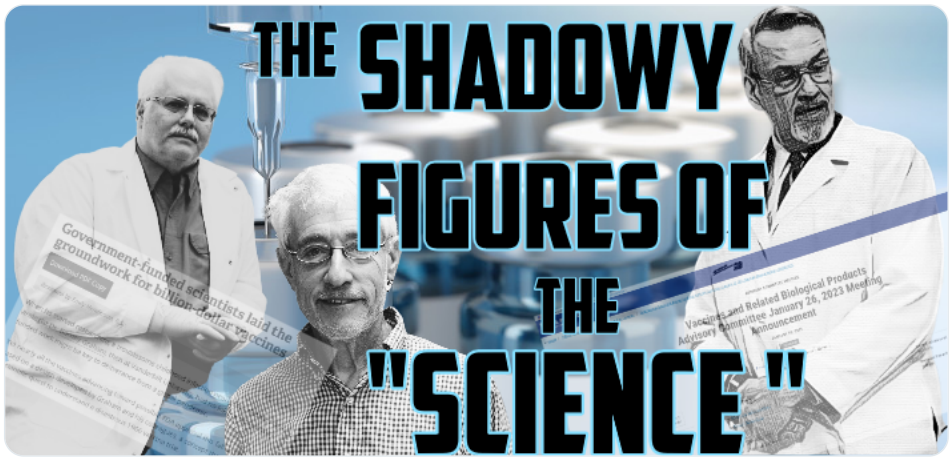
Destiny Rezendes @dezzie_rezzie

Oct 19, 2023 · 13 tweets · dezzie_rezzie/status/1714799882542718983

1🧵Ralph Baric has been silent throughout the pandemic but it's not for a lack of activity. From the moment the pandemic began, Baric was proactive in shaping the narrative. 55 days after the WHO declared a global pandemic he co-authored a very important paper.



2🧵According the title it was a summary report for CEPI/BC March 12–13, 2020 meeting. Which took place one day after the pandemic was declared. The rest of the title reads: Assessment of risk of disease enhancement with COVID-19 vaccines.

Consensus summary report for CEPI/BC March 12–13, 2020 meeting: Assessment of risk of disease enhancement with COVID-19 vaccines

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3🧵The paper, submitted May 5th 2020, bares amongst the author list Ralph Baric, Stanley Perlman, and Barney Graham among others. The paper acknowledges funding in part by CEPI [Bill & Melinda +WHO's epidemic preparedness company.]

Consensus summary report for CEPI/BC March 12–13, 2020 meeting: Assessment of risk of disease enhancement with COVID-19 vaccines

Paul-Henri Lambert [a], Donna M. Ambrosino [b], Svein R. Andersen [c], Ralph S. Baric [d], Steven B. Black [e], Robert T. Chen [e], Cornelia L. Dekker [e,*], Arnaud M. Didierlaurent [a], Barney S. Graham [g], Samantha D. Martin [h], Deborah C. Molrine [i], Stanley Perlman [j], Philip A. Picard-Fraser [k], Andrew J. Pollard [l], Chuan Qin [f], Kanta Subbarao [m], Jakob P. Cramer [n]

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ABSTRACT

A novel coronavirus (CoV), Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in late 2019 in Wuhan, China and has since spread as a global pandemic. Safe and effective vaccines are thus urgently needed to reduce the significant morbidity and mortality of Coronavirus Disease 2019 (COVID-19) disease and ease the major economic impact. There has been an unprecedented rapid response by vaccine developers with now over one hundred vaccine candidates in development and at least six having reached clinical trials. However, a major challenge during rapid development is to avoid safety issues both by thoughtful vaccine design and by thorough evaluation in a timely manner. A syndrome of "disease enhancement" has been reported in the past for a few viral vaccines where those immunized suffered increased severity or death when they later encountered the virus or were found to have an increased frequency of infection. Animal models allowed scientists to determine the underlying mechanism for the former in the case of Respiratory syncytial virus (RSV) vaccine and have been utilized to design and screen new RSV vaccine candidates. Because some Middle East respiratory syndrome (MERS) and SARS-CoV-1 vaccines have shown evidence of disease enhancement in some animal models, this is a particular concern for SARS-CoV-2 vaccines. To address this challenge, the Coalition for Epidemic Preparedness Innovations (CEPI) and the Brighton Collaboration (BC) Safety Platform for Emergency vACcines (SPEAC) convened a scientific working meeting on March 12 and 13, 2020 of experts in the field of vaccine immunology and coronaviruses to consider what vaccine designs could reduce safety concerns

Abbreviations: ACE2, Angiotensin-converting enzyme 2; ADE, Antibody disease enhancement; ARDS, Acute respiratory distress syndrome; B/HPIV3, Bovine/human parainfluenza virus type 3; BC, Brighton Collaboration; BPL, β-Propiolactone; BtCoV, Bat coronavirus; CEPI, Coalition for Epidemic Preparedness Innovations; CNS, Central nervous system; COVID-19, Coronavirus Disease 2019; CRISPR, Clustered regularly interspaced short palindromic repeats; DNA, Deoxyribonucleic acid; DPP4, Dipeptidyl peptidase-4; hACE2, Human ACE2 receptor; HBs, Hepatitis B surface antigen; hDPP4, Human DPP4; IHC, Immunohistochemistry; MERS CoV, Middle East respiratory syndrome coronavirus; mRNA, Messenger RNA; MVA, Modified Vaccinia Virus Ankara; NHP, Non-human primate; Non-SPF, Non-specific pathogen free; NTD, N terminal domain; RAG1, Recombination activating gene 1; RBD, Receptor binding domain; rMVA, Recombinant modified vaccinia virus Ankara; RNA, Ribonucleic acid; RSV, Respiratory syncytial virus; SARS-CoV-1, Severe acute respiratory syndrome coronavirus 1; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; SPEAC, Safety Platform for Emergency vACcines; TCR, T-cell receptor; Tg, Transgenic; Th1, T-helper cell type 1; Th2, T-helper cell type 2; VSV, Vesicular stomatitis virus; WHO, World Health Organization.

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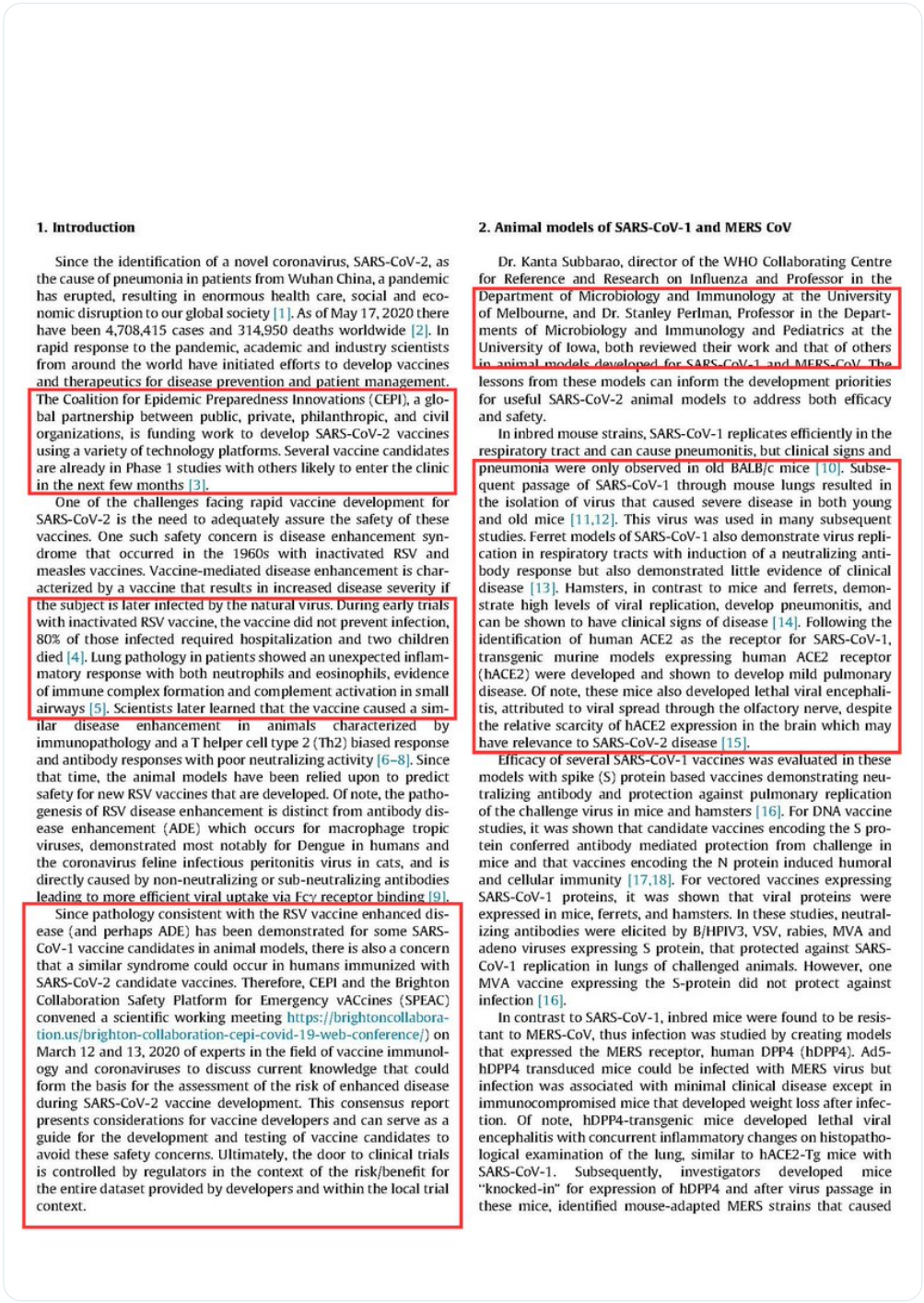

1. Introduction

Since the identification of a novel coronavirus, SARS-CoV-2, as the cause of pneumonia in patients from Wuhan China, a pandemic has erupted, resulting in enormous health care, social and economic disruption to our global society [1]. As of May 17, 2020 there have been 4,708,415 cases and 314,950 deaths worldwide [2]. In rapid response to the pandemic, academic and industry scientists from around the world have initiated efforts to develop vaccines and therapeutics for disease prevention and patient management. The Coalition for Epidemic Preparedness Innovations (CEPI), a global partnership between public, private, philanthropic, and civil organizations, is funding work to develop SARS-CoV-2 vaccines using a variety of technology platforms. Several vaccine candidates are already in Phase 1 studies with others likely to enter the clinic in the next few months [3].

One of the challenges facing rapid vaccine development for SARS-CoV-2 is the need to adequately assure the safety of these vaccines. One such safety concern is disease enhancement syndrome that occurred in the 1960s with inactivated RSV and measles vaccines. Vaccine-mediated disease enhancement is characterized by a vaccine that results in increased disease severity if the subject is later infected by the natural virus. During early trials with inactivated RSV vaccine, the vaccine did not prevent infection, 80% of those infected required hospitalization and two children died [4]. Lung pathology in patients showed an unexpected inflammatory response with both neutrophils and eosinophils, evidence of immune complex formation and complement activation in small airways [5]. Scientists later learned that the vaccine caused a similar disease enhancement in animals characterized by immunopathology and a T helper cell type 2 (Th2) biased response and antibody responses with poor neutralizing activity [6–8]. Since that time, the animal models have been relied upon to predict safety for new RSV vaccines that are developed. Of note, the pathogenesis of RSV disease enhancement is distinct from antibody disease enhancement (ADE) which occurs for macrophage tropic viruses, demonstrated most notably for Dengue in humans and the coronavirus feline infectious peritonitis virus in cats, and is directly caused by non-neutralizing or sub-neutralizing antibodies leading to more efficient viral uptake via Fcγ receptor binding [9].

Since pathology consistent with the RSV vaccine enhanced disease (and perhaps ADE) has been demonstrated for some SARS-CoV-1 vaccine candidates in animal models, there is also a concern that a similar syndrome could occur in humans immunized with SARS-CoV-2 candidate vaccines. Therefore, CEPI and the Brighton Collaboration Safety Platform for Emergency vACcines (SPEAC) convened a scientific working meeting https://brightoncollaboration.us/brighton-collaboration-cepi-covid-19-web-conference/) on March 12 and 13, 2020 of experts in the field of vaccine immunology and coronaviruses to discuss current knowledge that could form the basis for the assessment of the risk of enhanced disease during SARS-CoV-2 vaccine development. This consensus report presents considerations for vaccine developers and can serve as a guide for the development and testing of vaccine candidates to avoid these safety concerns. Ultimately, the door to clinical trials is controlled by regulators in the context of the risk/benefit for the entire dataset provided by developers and within the local trial context.

2. Animal models of SARS-CoV-1 and MERS CoV

Dr. Kanta Subbarao, director of the WHO Collaborating Centre for Reference and Research on Influenza and Professor in the Department of Microbiology and Immunology at the University of Melbourne, and Dr. Stanley Perlman, Professor in the Departments of Microbiology and Immunology and Pediatrics at the University of Iowa, both reviewed their work and that of others in animal models developed for SARS-CoV-1 and MERS-CoV. The lessons from these models can inform the development priorities for useful SARS-CoV-2 animal models to address both efficacy and safety.

In inbred mouse strains, SARS-CoV-1 replicates efficiently in the respiratory tract and can cause pneumonitis, but clinical signs and pneumonia were only observed in old BALB/c mice [10]. Subsequent passage of SARS-CoV-1 through mouse lungs resulted in the isolation of virus that caused severe disease in both young and old mice [11,12]. This virus was used in many subsequent studies. Ferret models of SARS-CoV-1 also demonstrate virus replication in respiratory tracts with induction of a neutralizing antibody response but also demonstrated little evidence of clinical disease [13]. Hamsters, in contrast to mice and ferrets, demonstrate high levels of viral replication, develop pneumonitis, and can be shown to have clinical signs of disease [14]. Following the identification of human ACE2 as the receptor for SARS-CoV-1, transgenic murine models expressing human ACE2 receptor (hACE2) were developed and shown to develop mild pulmonary disease. Of note, these mice also developed lethal viral encephalitis, attributed to viral spread through the olfactory nerve, despite the relative scarcity of hACE2 expression in the brain which may have relevance to SARS-CoV-2 disease [15].

Efficacy of several SARS-CoV-1 vaccines was evaluated in these models with spike (S) protein based vaccines demonstrating neutralizing antibody and protection against pulmonary replication of the challenge virus in mice and hamsters [16]. For DNA vaccine studies, it was shown that candidate vaccines encoding the S protein conferred antibody mediated protection from challenge in mice and that vaccines encoding the N protein induced humoral and cellular immunity [17,18]. For vectored vaccines expressing SARS-CoV-1 proteins, it was shown that viral proteins were expressed in mice, ferrets, and hamsters. In these studies, neutralizing antibodies were elicited by B/HPIV3, VSV, rabies, MVA and adeno viruses expressing S protein, that protected against SARS-CoV-1 replication in lungs of challenged animals. However, one MVA vaccine expressing the S-protein did not protect against infection [16].

In contrast to SARS-CoV-1, inbred mice were found to be resistant to MERS-CoV, thus infection was studied by creating models that expressed the MERS receptor, human DPP4 (hDPP4). Ad5-hDPP4 transduced mice could be infected with MERS virus but infection was associated with minimal clinical disease except in immunocompromised mice that developed weight loss after infection. Of note, hDPP4-transgenic mice developed lethal viral encephalitis with concurrent inflammatory changes on histopathological examination of the lung, similar to hACE2-Tg mice with SARS-CoV-1. Subsequently, investigators developed mice "knocked-in" for expression of hDPP4 and after virus passage in these mice, identified mouse-adapted MERS strains that caused

4🧵You should know that Barney Graham one of the authors is a lead scientists at NIH's Vaccine Research Center and partial but key contributor to the current Covid-19 Vaccines. Because of him, in part, the NIH was awarded $400M from Moderna for their help designing the C19 jab.

Barney Graham:

Barney Graham played a significant role in the creation of the COVID-19 vaccines. He is a renowned virologist and deputy director of the Vaccine Research Center within the National Institutes of Health (NIH) [1][2][3][4]. Graham and his team had been studying the nooks and crannies of spike-covered coronaviruses for nearly a decade before the pandemic began [2]. They had been working on building a library of prototype vaccines against each of the major virus families known to be capable of spawning a human outbreak. The research could be pulled off the shelf if a virus emerged and tweaked to fight the new threat [2]. Graham's work with other scientists on coronaviruses paved the way for vaccines [2]. He oversaw the work at the NIH's Vaccine Research Center that provided the basis for designing and evaluating the initial COVID-19 vaccines and antibodies [4]. Graham had also forged a relationship with an up-and-coming biotechnology company, Moderna, that could design vaccines fast [2]. His lifelong effort to increase diversity in science had culminated in a team of Black scientists who were ready to go [2]. Overall, Graham's work and research were instrumental in the development of the COVID-19 vaccines.

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Schaefer Edwards - Dec. 15, 2021
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Barney Graham '75 named a Time Hero of the Year for developing COVID-19 vaccine

Rice alumnus Barney Graham '75, a renowned virologist and deputy director of the Vaccine Research Center within the National Institutes of Health (NIH), has been named a 2021 Hero of the Year by Time magazine for his work developing Moderna's groundbreaking COVID-19 vaccine.

Government-funded scientists laid the groundwork for billion-dollar vaccines

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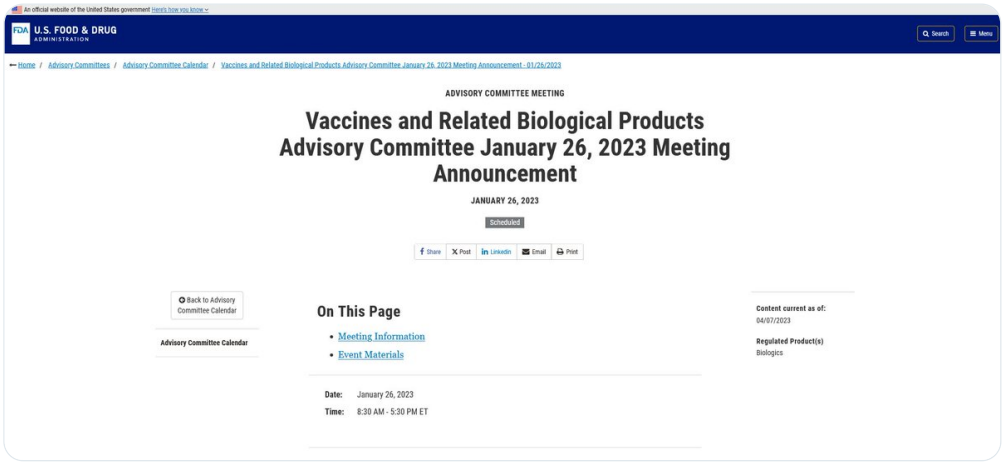
Reviewed by Emily Henderson, B.Sc. Nov 18 2020

When he started researching a troublesome childhood infection nearly four decades ago, virologist Dr. Barney Graham, then at Vanderbilt University, had no inkling his federally funded work might be key to deliverance from a global pandemic.

Yet nearly all the vaccines advancing toward possible FDA approval this fall or winter are based on a design developed by Graham and his colleagues, a concept that emerged from a scientific quest to understand a disastrous 1966 vaccine trial.

5🧵Perlman is one of the 15 members of the Vaccines and Related Biological Products Advisory Committee which was instrumental in the approval of the Covid-19 Vaccines at the FDA. Baric, as we all know is the leading world's expert on GOF coronaviruses research.



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ADVISORY COMMITTEE MEETING

Vaccines and Related Biological Products Advisory Committee January 26, 2023 Meeting Announcement

JANUARY 26, 2023

Scheduled

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Date: January 26, 2023

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Content current as of: 04/07/2023

Regulated Product(s) Biologics

Food and Drug Administration
Center for Biologics Evaluation and Research
SUMMARY MINUTES
178th VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE
January 26, 2023

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Darin Edwards, Ph.D. - Moderna
Filip Dubovsky, M.D. - Novavax
Heather Scobie, Ph.D., M.PH. – CDC
Jefferson Jones, M.D., MPH, FAAP - CDC
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Rituparna Das, M.D., Ph.D.- Moderna
Ruth Link-Gelles, Ph.D. -CDC
Tom Shimabukuro, M.D., MPH, MBA - CDC

FDA Participants
Peter W. Marks, M.D., Ph.D. - Speaker
David C. Kaslow, M.D. - Speaker
Jerry Weir, Ph.D. -Speaker
Richard Forshee, Ph.D. - Speaker
Sudhakar Agnihothram, B. Pharm., Ph.D.
Maria Allende, M.D.

+Not Attending
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*>Acting Consumer Rep
***Industry Representative

Stanley Perlman, MD, a professor of microbiology and immunology at the University of Iowa, has been a leading figure in the response to the COVID-19 pandemic. Perlman has studied coronaviruses for 38 years and has been instrumental in advancing our understanding of the virus and developing treatments and vaccines [1][2][3]. Here are some of the impacts that Perlman has made in the response to the COVID-19 pandemic:

- Perlman's research on coronaviruses has been critical in advancing our understanding of the virus and developing treatments and vaccines [1][2][3][5].
- Perlman has been a leading voice in the scientific community, providing insights and guidance on the pandemic [1][3][6].
- Perlman has been featured in numerous media outlets, including On Point and YouTube, where he has shared his expertise on the pandemic [3][6].
- Perlman has co-authored several papers on COVID-19, including a paper on immune dysregulation and immunopathology induced by SARS-CoV-2 and related coronaviruses [4].
- Perlman has been involved in efforts to develop treatments and vaccines for COVID-19, including serving as a member of the scientific advisory board for the COVID-19 Prevention Network [1].
- Perlman's work has been critical in advancing our understanding of the similarities and differences between COVID-19 and other coronaviruses, such as SARS and MERS [5].

Overall, Perlman's work has been instrumental in advancing our understanding of COVID-19 and developing treatments and vaccines for the virus. His expertise and guidance have been critical in the response to the pandemic.

6🧵The paper is supposed to help policy makers & pharma w/ the best approach to the jabs were. They admit, multiple studies have shown evidence of disease enhancement in vaccinated animals after challenge w/live virus & there is some evidence of ADE in human primary monocytes.

- The highlighted text describes the results of studies conducted on two different animal models, human ACE2 transgenic mice and rhesus macaques, infected with SARS-CoV-2.
- The hACE2 Tg mice were observed to express the human ACE2 protein in various tissues including the lung, heart, kidney, and intestine. Upon intranasal inoculation with SARS-CoV-2, the mice experienced weight loss and viral RNA was detected in the lungs and intestine.

To address this challenge, a scientific working meeting was convened by the Coalition for Epidemic Preparedness Innovations (CEPI) and the Brighton Collaboration (BC) Safety Platform for Emergency vACcines (SPEAC) on March 12 and 13, 2020. Experts in the field of vaccine immunology and coronaviruses were brought together to consider vaccine designs that could reduce safety concerns.

Finally, it is noted that there has not been an agreed upon positive control applied in these animal studies, and thus interpretations are hampered.

more severe disease and increased histopathology with more pulmonary edema than those infected with the original MERS strain [19]. Importantly, mice without functional T cells, such as RAG1-/- and TCR alpha-/-, had delayed viral clearance whereas mice that could not produce antibodies, muMT mice, did not show delay in clearance. Similar models were developed by CRISPR/Cas9 mutagenesis of two residues in the mouse ACE2 molecule, followed by mouse adaptation with serial passage, leading to an ARDS model of lethal infection [20,21]. Taken together this evidence supports the notion that T cells are important in viral clearance for MERS [22].

Non-human primate (NHP) models have also been established for both SARS-CoV-1 and MERS-CoV. There was evidence of upper respiratory and lower respiratory tract SARS-CoV-1 replication in African green monkeys to a greater extent than in cynomolgus macaques, and least in rhesus macaques, with little evidence of clinical disease in all three species [23]. Of note, consistent with findings in older humans and mice, increased pathology has been documented in aged cynomolgus macaques with SARS-CoV-1 wild type infection [24]. There is some controversy on the disease severity in the MERS models with different groups seeing different levels of pathology. This has not been resolved [25,26].

3. Enhanced disease following SARS-CoV-1 vaccines

Both vaccine efficacy and safety have been studied in animal models with many SARS-CoV-1 candidate vaccines. The group of experts discussed how the vaccine models were utilized to characterize the response of specific vaccines and to examine both disease enhancement and antibody dependent enhancement (ADE) signals.

There is evidence for disease enhancement in vaccinated animals after challenge with live virus in multiple studies with SARS–CoV-1 vaccine candidates as summarized in Table 1. We are limiting our comments in this report to data in animal models and not discussing *in vitro* data except to mention that there is some evidence of ADE in human primary monocytes [27,28]. Different animal models exhibit different pulmonary pathology but generally are characterized by cellular infiltrates including eosinophils. In this summary, we provide an overview of the consensus opinion on vaccine related outcomes in animal models that were of concern for risk of disease enhancement and could guide assessments of SARS-CoV-2 vaccine candidates.

In murine models, evidence for vaccine related disease enhancement has been demonstrated for inactivated whole vaccine (with and without alum), vectored vaccine expressing N protein (but not seen with vectored vaccine expressing S protein in same report), a replicon particle platform expressing S protein, and a vectored vaccine expressing S proteins. In general, the pathology described included pulmonary infiltrates often with eosinophils observed. Th2 dominant responses were documented in some reports by expression of Th2 driven cytokines [29–33]. In a ferret model, hepatitis was demonstrated in animals vaccinated with a recombinant modified vaccinia virus Ankara vaccine expressing S protein and then challenged with virus [34] although questions have been raised about this study [35].

Of note, mouse models have also shown evidence of enhanced disease for inactivated and recombinant adenovirus 5-based MERS-CoV vaccine [36,37].

Non-human primate models have also produced evidence of enhanced disease after SARS-CoV-1 vaccine immunization. Chinese macaques immunized with a modified vaccinia virus expressing S protein then challenged with SARS-CoV-1 did not develop clinical disease, but histopathology showed lung injury. This injury was characterized by decreased wound healing, and increased pro-inflammatory macrophages expressing IL-6, IL-8, and CCL2 [38]. This report also demonstrated that passively administered anti-S antibody was associated with lung pathology after challenge with the live virus although the mechanism may not be through Fc receptor and thus not classic "ADE". Of note, a second report similarly demonstrates the effect with certain anti-S antibody preparations and without Fc involvement [39,40]. The relevance of these reports remains unclear as there are multiple studies with administration of neutralizing monoclonal antibodies to different models that did not induce disease enhancement. Other investigators have reported absence of disease enhancement in both hamsters and monkeys immunized with a whole inactivated vaccine although these models differed in a number of ways, most notably by the use of BPL (β-Propiolactone) instead of formalin for inactivation of the virus [41,42]. Finally, we note that there has not been an agreed upon positive control applied in these animal studies and thus interpretations are hampered.

4. SARS-CoV-2 murine and NHP models newly developed

Animal models with SARS-CoV-2 are being rapidly developed by multiple research groups. Dr. Qin Chuan, Professor and Director

Table 1
Evidence of enhanced disease in SARS-CoV-1 vaccine candidates.

Animal Model	Vaccine	Adjuvant	Immunopathology	Reference
Murine[1]	VEE Replicon Particles expressing N protein	–	YES	Deming 2006
Murine[2]	Recombinant Vaccinia virus expressing N protein	–	YES	Yasui 2008
Murine[2]	Inactivated Whole Virus	Alum	YES	Bolles 2011
		–	YES	
Murine[4]	Replicon Particles expressing S protein	–	YES	Sheahan 2011
Murine[2]	Inactivated Whole Virus and S protein vaccines	Alum	YES	Tseng 2012
		–	YES	
Ferret[6]	Recombinant Modified Vaccinia Virus Ankara (rMVA) expressing S protein	–	YES[†]	Weingartl 2004
NHP[7]	Modified Vaccinia Ankara (MVA) virus encoding full-length S protein	–	YES	Liu 2019
	Passive anti-S sera	N/A	YES	
NHP[7]	Inactivated Whole Virus	–	YES	Wang 2016/2020
	Passive Human SARS Antiserum	N/A	YES	

[1] Young and senescent female BALB/c mice.
[2] BALB/c mice.
[3] Aged BALB/c mice.
[4] Young and aged BALB/c mice.
[5] Female BALB/c mice.
[6] *Mustela putorius furo*, castrated males.
[7] Chinese rhesus macaque.
[†] Acute hepatitis.

of the Institute of Laboratory Animal Science, Comparative Medicine Center of the Peking Union Medical College presented data on SARS-CoV-2 infection in both transgenic mice and rhesus macaque models.

Human ACE2 transgenic mice (hACE2 Tg) aged 4–6 weeks and 6–11 months of age were studied and hACE2 expression was observed in lung, heart, kidney and intestinal tissues. Following intranasal inoculation with SARS-CoV-2, weight loss was observed, and viral RNA was detected in the lungs as well as in the intestine [43].

Gross pathology demonstrated swollen and enlarged lungs with moderate interstitial pneumonia. Histological studies documented an accumulation of inflammatory cells including monocytes and lymphocytes in alveolar interstitium, with thickening of alveolar walls. SARS-CoV-2 S protein was detected by IHC in alveolar macrophages and epithelia [43].

NHP were also infected with SARS-CoV-2 with 3 rhesus macaques aged 3–4 years inoculated intratracheally and although no fever was observed, weight loss and asthenia were seen on multiple days. Viral RNA was detected from nasal and throat swabs and to a lesser degree in anal specimens, peaking on days 3 to 7 and lasting until day 11 post infection. One animal was euthanized on day 7 for necropsy and viral RNA was detected in multiple organs including CNS, skeletal muscle and heart. For the two surviving rhesus macaques, positive neutralization titers were documented by day 11 post infection. There was radiographic evidence of multiple ground glass opacities in the lungs on days 3, 5 and 7 post infection. Microscopically the lung lesions represented an acute interstitial pneumonia characterized by mild to moderate thickening of alveolar septum, increased number of macrophages, degeneration of pneumocytes and an inflammatory cell infiltration. Presence of viral antigen was confirmed, predominately in alveolar monocytes and macrophages [44]. Analysis of blood samples showed a decline in counts of total white blood cells, lymphocytes and monocytes with no observed changes in percentages. A decrease in both CD3 + CD4 + and CD3 + CD8 + T-cell counts was observed. Importantly, these hematological findings are similar to those seen in SARS-CoV-2 infected patients.

This model could serve as a critical tool for detailed studies of pathogenesis and the evaluation of intervention strategies including vaccines. Of note, following the meeting another group has confirmed SARS-CoV-2 infection in rhesus macaques with viral antigen detected in type I and type II pneumocytes and diffuse pulmonary alveolar damage noted [45]. Experts agreed that these models and others under development should be utilized to evaluate vaccine candidates for any evidence of disease enhancement as specified in later sections.

5. COVID-19 vaccine design considerations for efficacy and safety

5.1. Structure and function of S glycoproteins in coronavirus

Design of safe and effective COVID-19 vaccines can be informed by knowledge of previous coronavirus vaccine development activities and shared elements of viral pathogenesis for non-coronaviruses such as RSV. Specific epitope targets for potent neutralizing antibody, platforms for inducing both neutralizing antibody and effective T cell responses, and adjuvants for improving immunogenicity were presented at the conference. We review first the structure and function of the major target of COVID-19 vaccines, spike (S) glycoprotein.

Ralph Baric PhD, Professor in the Department of Epidemiology at the University of North Carolina Chapel Hill School of Medicine presented a review of the structure and function of coronavirus (CoV) S glycoprotein highlighting priorities for the development of vaccine and immune therapeutics. There is a long history of emerging CoVs with acceleration of cross-species movement and emergence of highly pathological strains in the last 16 years, including SARS-CoV-1, MERS-CoV, and SARS-CoV-2, and this trend is likely to increase in the future. Phylogenetic relationships within CoVs have been established, and Group 2B includes SARS-CoV-1 and SARS-like CoVs including SARS-CoV-2, BtCoV WIV1 and BtCoV SHC014. Similarly, Group 2C are MERS-like CoVs which are also poised for human emergence. Within Group 2B, known SARS-like CoVs are divided into high or low pre-epidemic potential. High risk features include use of ACE2 for cell entry, growth in primary human airway cells, causing ARDS, causing age-related disease severity, and escape from existing immune therapeutics. Drivers of CoV evolution include the high mutation rate of the RNA-dependent RNA polymerase paired with the regulated fidelity complex. CoVs also demonstrate high rates of RNA recombination as during mixed infection up to 25% of progeny are recombinant, and modular evolution allows CoVs to swap whole genes or portions of key proteins between strains. The S protein itself, which regulates host range, tissue tropism, and transmissibility, can tolerate a high mutation rate while retaining its function.

The organization of the SARS-CoV-2 genome has been elucidated and SARS-CoV-2, like SARS-CoV-1, has been shown to use hACE2 for cell entry. Group 2B viruses have fourteen contact interfaces between their S protein and ACE2. Variation across the interface sites can facilitate orthologous species ACE2 receptor usage, since as few as seven interface sites are needed for entry. The prefusion structure of the S glycoprotein has three major antigenic domains, receptor binding domain (RBD), N terminal domain (NTD), and S2. Epitopes on SARS-CoV-1 RBD have been identified as targets for neutralizing antibodies. Analyzing the variations and conserved regions in the S protein of Group 2B SARS-like CoVs, shows conserved sites on the S2 region that could be targeted in broad-based therapeutics against multiple CoVs.

Dr. Baric stressed that there is a large reservoir of SARS-like and MERS-like CoVs poised for emergence in humans. Two priorities are immediate vaccine candidates specific for SARS-CoV-2 and development of broad-based vaccines protective against antigenically distinct CoVs destined to emerge in the future. Key priorities for the development of a SARS-CoV-2 vaccine include characterization the SARS-CoV-2 neutralizing epitope map, identification of broadly cross-reactive neutralizing epitopes, identification of putative enhancing epitopes that might potentiate disease *in vivo*, identification of key T cell epitopes across outbred populations, and determination of correlates of protective immunity.

5.2. Preserving neutralization sensitive epitopes on spike proteins

Barney Graham, MD PhD, Deputy Director of the NIH Vaccine Research Center presented data on the immunogenicity and neutralizing efficacy of truncated spike (S) antigens, with a focus on SARS-CoV-2. Class I fusion proteins (such as S protein) are common among enveloped viruses including RSV, parainfluenza viruses, and coronaviruses and have been successfully stabilized in their prefusion conformations. This approach has been shown to preserve neutralization-sensitive epitopes, avoid antibodies that are non-neutralizing, and improve expression in transfected cells, thus aiding in manufacturing and immunogenicity of gene-based vectors. The S proteins of SARS-CoV-1 and MERS-CoV have both been successfully stabilized by introducing two proline residues to the top of the central helix, preventing heptad assembly and stabilizing the S2 region and the entire S protein as a result (Fig. 1) [46].

The SARS-CoV-2 S protein structure was solved shortly after its emergence and shows similar structure and mobility as the SARS-CoV-1 S [47]. The timing from first knowledge of SARS-CoV-2 to the

7🧵Despite the many unknowns the group of "so-called" experts insist that the presence of disease enhancement in animal models after viral challenge should not be the sole reason to halt the progress of a candidate vaccine into early clinical trials for COVID-19.

Given the unprecedented demand for an effective vaccine, the use of adjuvants may be critical for subunit vaccines in providing antigen-dose sparing, increased immunogenicity, breadth and duration of response, potentially eliciting cross-protection against new CoV strains and minimizing the risk of enhanced disease.

7. Consensus considerations on the assessment of the risk of disease enhancement with COVID-19 Vaccines:

Following the presentations, attendees participated in discussion of the suggested consensus statements and all attendees were asked to comment on the draft statements available online. These comments were reviewed and discussed again on the second day of the meeting and resulted in the summary consensus statement that follows.

Murine models for assessment of vaccine-related disease enhancement

- SARS-CoV-2 has a low affinity for murine ACE2 receptor and murine models will require the use of hACE2 transgenic mice, preferably with a 'knock-in' approach. Preliminary data indicate the possibility of infecting hACE2 transgenic mice with demonstration of viral replication and mild lung lesions. Mouse adaptation of SARS-CoV-2, as done with SARS-CoV-1, will likely be required to obtain a virus that causes more severe disease in mice. Models that develop acute lung injury with some lethality and that mimic the human condition will be important for evaluating vaccine safety.
- Previous studies from SARS-CoV-1 and MERS-CoV indicated that some vaccines, especially those using whole inactivated virus, could enhance the disease induced in mice challenged with SARS-CoV-1 or MERS-CoV. The lung lesions were highly inflammatory, with a dominance of eosinophil infiltration and occurred in animals despite presence of a neutralizing antibody response and reduced challenge virus replication in the lungs. Such studies have not yet been completed for SARS-CoV2.
- In mice, this immunopathology was considered a consequence of a dominant Th2 type response to the vaccine antigens. It was not seen after including adjuvants (e.g. CpG) in the vaccine or other vaccine formulations known to drive immune responses towards Th1. The timing of challenge after vaccination may be critical. It would be of major interest to explore the outcome following challenge at later timepoints when antibodies are significantly decaying.
- One should be aware of the potential confounding effect of cell-culture excipients in the vaccine and challenge strain material. It is known that impurities such as fetal calf serum in the preclinical vaccine preparation may induce eosinophil influx in any mouse model if the challenge strain also contains the same excipients.
- In these models, characterization of the immune response to the candidate vaccine (e.g., IgG isotypes, Th2 markers) may have some predictive value.
- Other small animal models which can be infected by SARS-CoV-2 can be considered (e.g. ferret, hamster). Development of small animal models of severe disease will also inform studies of vaccine-enhanced disease.

Non-human primate models for assessment of vaccine-mediated enhanced disease

- Non-human primates (NHP) are of primary interest in view of their ACE2 homology with hACE2. Preliminary studies indicate the possibility of inducing some COVID-19 lung pathological features after infection, without clinical signs, in Rhesus macaques. African Green monkeys may be more susceptible to COVID-19, but the model suffers from some limitations (e.g. access, genetic polymorphism).
- Previous studies with SARS candidate vaccines have suggested a risk of enhanced pathology in NHPs after viral challenge. Eosinophilic infiltrates were not prominent. The mechanism is still incompletely defined but there is evidence for a role of non-neutralizing antibodies. Non- or incompletely neutralizing antibodies may contribute to:
  - the formation of pathogenic immune complexes and
  - Fc-mediated viral capture by monocytes/macrophages that may favor excessive T-cell activation and inflammation.
- Enhanced pathology was seen following passive transfer of IgG from immunized NHPs

General considerations on animal models

- Although existing animal models of COVID-19 imperfectly reproduce the human disease, they appear useful for assessing the risk of disease enhancement. Vaccine responses are closer to human responses in NHPs than in mice. Therefore, it is likely that data obtained from NHP studies are more significant. However, there is an urgent need to standardize the NHP model (read-out of disease enhancement, timing of challenge, age) and to include appropriate controls (i.e., a vaccine that induces enhanced pathology and disease) and a sufficient number of animals to be confident of findings in outbred species. It is important to control for potential co-infection, including with other coronaviruses, in all non-SPF models.
- Potential markers of safety in these animal models could include:
  - the relative levels of neutralizing vs non-neutralizing antibodies,
  - antibody affinity,
  - T-cell response profile,
  - quantitative virology in the upper and lower respiratory tract
  - characterization of lung histopathology with immunohistochemistry for viral antigen and immune cell markers.
- Passive transfer in NHPs of human antibodies generated during Phase 1 trials, followed by viral challenge could be considered to assess the risk of disease enhancement.
- Challenge of immunized animals with a closely related heterologous CoV strains may assess the risk of enhancement during future outbreaks.
- In case of disease enhancement, in-depth studies in animal models may give some indications on the mechanism of immunopathology. They can inform human trial designers on the critical immunological risk markers to be monitored in Phase 1 trials.
- Based on previous experience with SARS and other viral diseases, it may be useful to evaluate the risk of disease enhancement for COVID-19 vaccines (particularly those including whole virions or N protein) in an established NHP model before advanced clinical development.

During the Vaccine Design session, the group of Experts suggested that consideration should be given to the following:

- Caution should be observed when developing vaccines to avoid inducing predominant Th2 responses and non-neutralizing antibodies.
- Vaccines inducing strong neutralizing antibodies, predominant Th1 responses and balanced CD4/CD8 and polyfunctional T cell responses are less likely to induce immunopathology.

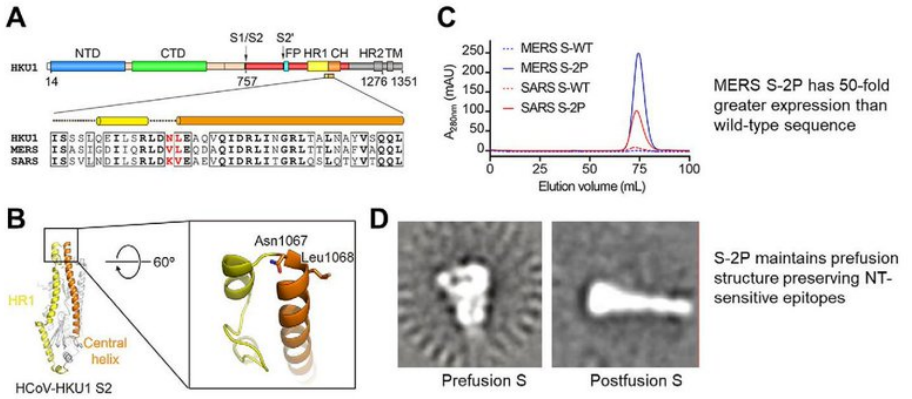


Fig. 1. 2P mutation stabilizes MERS and SARS CoV S; improves expression, prefusion structure, and immunogenicity.

beginning of the Phase 1 study was a remarkable sixty-five days. The advantages of mRNA vaccines include ability to create a highly precise type of protein to elicit the correct antibodies, to elicit T cell responses that are Th1 predominant, and the rapidity of manufacturing. Of course, disadvantages include the novel nature of both mRNA and DNA vaccines without any licensed vaccine with either technology to date and lack of experience for mass production. Therefore, multiple platforms for SARS-CoV-2 are under development that mitigate against some of the potential disadvantages of nucleic acid vaccines.

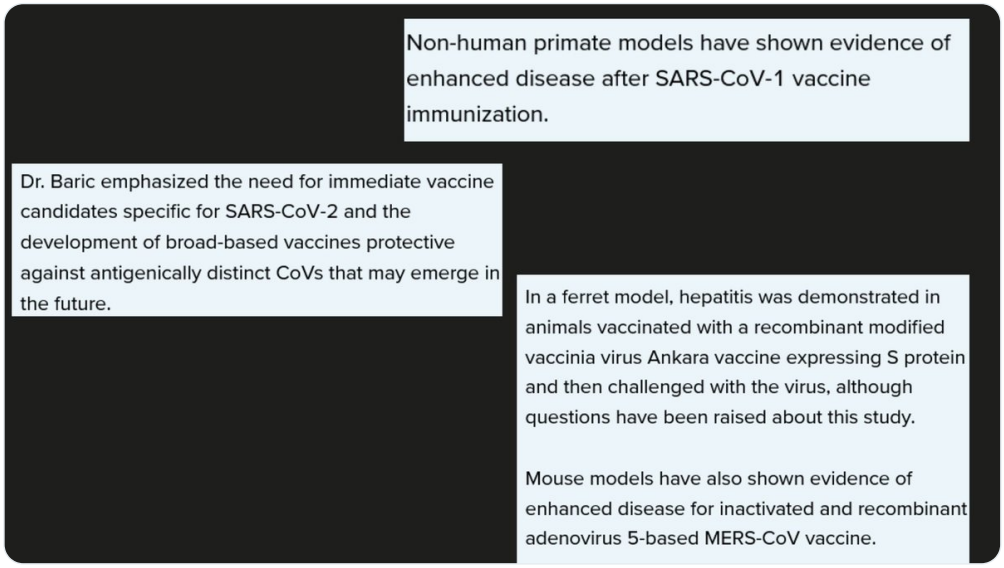
6. Effects of adjuvants on immune response and implications for COVID-19 vaccines

Although mRNA and DNA vaccines elicit T cell responses without adjuvants, adjuvants may be important for subunit and whole cell inactivated vaccines to increase their immunogenicity and drive an immune response that could limit the risk of disease enhancement. Multiple SARS-CoV-2 vaccines are in development including vectored vaccines, whole cell inactivated vaccines, and recombinant protein vaccines. The experts discussed how the choice of adjuvants will be important for both efficacy and safety with these platforms.

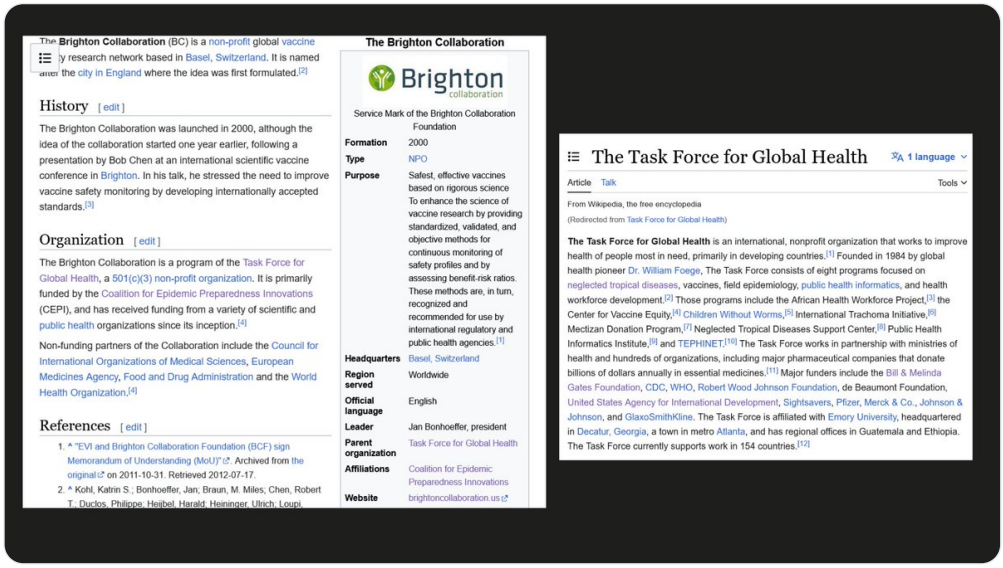
Dr. Arnaud Didierlaurent from the Centre of Vaccinology at the University of Geneva presented background on the effects of different adjuvants on animal and human immune responses. Several adjuvants are now being used in commercial vaccines or are in clinical development [48]. Oil-in-water emulsions such as MF59 or AS03 have been shown to increase the breadth of the antibody repertoire, binding affinity and affinity maturation when compared to unadjuvanted vaccines [49,50] In human studies with influenza vaccines, H5N1 vaccine adjuvanted with MF59 (squalene-based emulsion) increased the levels of H5-specific antibody for subclasses IgG1 and IgG3 and the binding to FcγR2 but not to FcγR3 when compared to alum adjuvanted vaccines. This demonstrates that the use of an adjuvant can skew the functionality profile of antigen-specific antibodies, with the potential to activate different innate effectors based on their FcγR expression [51]. Use of squalene-based emulsion vaccines for influenza have also been shown to increase CD4 + T cell response frequencies and cross-reactivity. Even if pre-existing cross-reactive antibodies are present prior to immunization, such adjuvants could activate naïve B cells and promote the adaptability of memory B cells [52–55].

In addition to antibodies, adjuvants can promote cellular responses. Human malaria challenge studies provided early evidence that the choice of adjuvants (combined with the malaria antigen RTS,S) was critical in achieving optimal protection and highlighted the importance of cellular response [56]. More recently, studies with Hepatitis B Surface Antigen (HBs) vaccine adjuvanted with AS01, AS03, AS04 or alum showed that vaccines formulated with AS01 and AS03 induced the highest antibody levels while AS01 promoted best HBs-specific CD4 T cell response [57]. These differences were associated with the magnitude of the initial inflammatory response triggered by the different adjuvanted formulations [57,58]. Interestingly, although the level of CD4 T cell response was lower in the alum group compared to the AS01 group, both adjuvants led to similar memory subset profiles and cytokine production profiles (polyfunctionality) and neither induced Th2 cytokines nor a CD8 induced response upon peptide restimulation. This indicates that use of alum may not necessarily lead to Th2 skewing in humans. Recently a number of systems biology studies have revealed that specific early signatures (e.g., interferon-dependent pathways) induced by adjuvanted vaccines are often associated with protective responses [59] but the impact of these early signals on functional features of antibodies and the quality of T cell response are not well established yet.

Although adjuvant selection is best performed in early clinical studies, animal models could be useful in determining the immune profile of adjuvanted vaccines. NHP models are well-established to assess immune responses to vaccination and elicit immune responses in closer parallel to humans than mice. For example, in non-human primates, adjuvant choice affects antibody half-life, antibody glycosylation and antibody binding to FcγRs, indicating effects on both antibody quality and function, like what is observed in humans [60]. When adeno-based vectored vaccines are given to humans or NHPs, both groups develop similar antibody function profiles. Additionally, NHPs and humans tend to show similarities in terms of "ranking" of adjuvants and innate immune pathways triggered by adjuvants. Overall, NHPs could be utilized to evaluate COVID-19 vaccine candidates with and without adjuvants and guide in the selection of vaccines that elicit desired attributes that could reduce the risk of vaccine-mediated enhanced disease.



8🧵The authors of the paper acknowledge financial support was provided by the Coalition for Epidemic Preparedness Innovations (CEPI) for their work under a service order entitled Safety Platform for Emergency vACcines (SPEAC) Project w/ the Brighton Collaboration.



9🧵Ralph Baric signed a Material Transfer Agreement w/Moderna in 2017. The same yr Barney Graham's team made a SARS vaccine breakthrough w/VRC [& later Moderna too] & Perlman was on the regulatory VRBPAC committee that authorized the C19 jabs.

Acknowledgement

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All authors attest they meet the ICMJE criteria for authorship.

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MATERIAL TRANSFER AGREEMENT

SIGNATURE PAGE

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Recipient's Investigator

Ralph Baric, PhD
Professor

Date: 12/12/2019

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Attention: Dr. Rachel Graham, Department of Epidemiology, University of North Carolina at Chapel Hill, 135 Dauer Drive, 2101 McGavran-Greenberg Hall, CB #7435, Chapel Hill, NC 27599-7435

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Duly Authorized

Jacqueline Quay
Director, Licensing & Innovation Support, OTC

Date: 12/16/19

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NIAID's Investigator

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Digitally signed by Amy F. Petrik -S
Date: 2019.12.12 08:05:22 -05'00'

PUBLIC HEALTH SERVICE

MATERIAL TRANSFER AGREEMENT

This Material Transfer Agreement ("MTA") has been adopted for use by the National Institutes of Health, the Food and Drug Administration and the Centers for Disease Control and Prevention, collectively referred to herein as the Public Health Service ("PHS") in all transfers of research material (Research Material) whether PHS is identified below as its Provider or Recipient.

Providers: *National Institute of Allergy and Infectious Diseases, National Institutes of Health ("NIAID")*
ModernaTX, Inc ("Moderna")

Recipient: The University of North Carolina at Chapel Hill

1. Provider agrees to transfer to Recipient's Investigator the following Research Material:

   mRNA coronavirus vaccine candidates developed and jointly-owned by NIAID and Moderna.

2. THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS. The Research Material will only be used for research purposes by Recipient's Investigator in his/her laboratory, for the research project described below, under suitable containment conditions. This Research Material will not be used for commercial purposes such as screening, production or sale, for which a commercialization license may be required. Recipient agrees to comply with all Federal rules and regulations applicable to the Research Project and the handling of the Research Material.

   a. Are the Research Materials of human origin?

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   b. If Yes in 2a, were Research Materials collected according to 45 CFR Part 46, "Protection of Human Subjects"?

   ___Yes Please provide Assurance Number: _____

Dr. Paydar read the voting results for the public record and then handed over the meeting to Dr. Perlman to ask the Committee for their Vote explanation. Dr. Perlman called upon each Committee Member in alphabetical order. Several members emphasized that harmonizing the composition of primary series and booster doses is an important step in improving vaccine uptake in all age groups.

Dr. Perlman then started the next session to discuss the two Discussion Topics as listed below:

Discussion Topic 1:
Future periodic vaccination campaigns:
***Simplification* of COVID-19 vaccine use:**
• *Immunization schedule*: Please discuss and provide input on simplifying the immunization schedule to authorize or approve a two-dose series in certain young children, and in older adults and persons with compromised immunity, and only one dose in all other individuals.
The committee agreed in principle that simplification of the immunization schedule was highly desirable and recommended that the simplification be based on the best available evidence.

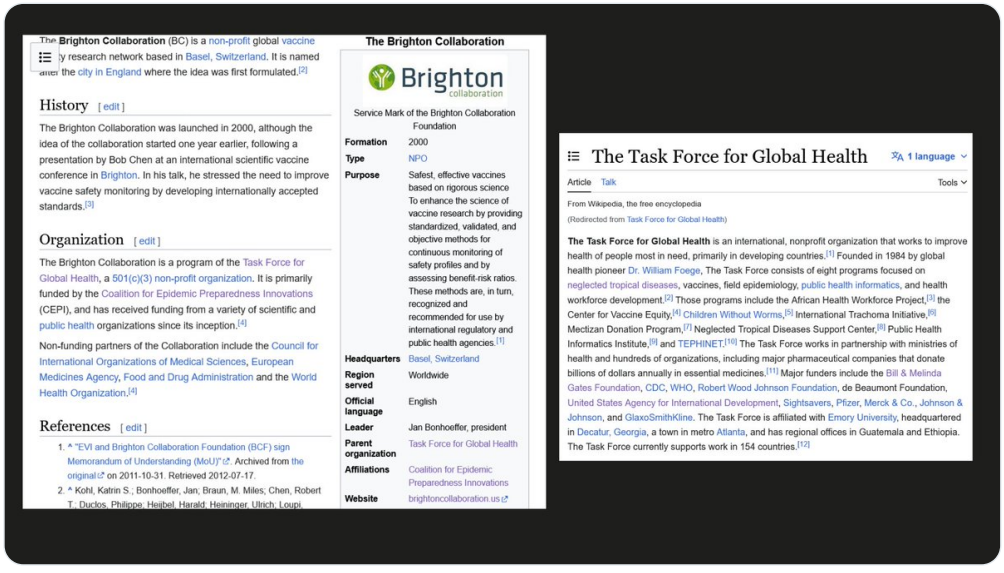
Discussion topic 2:
***Periodic update* to COVID-19 vaccines:**
• *Vaccine composition:* Please discuss and provide input on the consideration of periodic updates to COVID-19 vaccine composition, including to the currently authorized or approved vaccines to be available for use in the U.S. in the fall of 2023.
The committee agreed that periodic updates to COVID-19 vaccine strain composition would need to be considered annually, if not biannually, and that FDA and VRBPAC need to be prepared for urgent updates if escape variant strains emerge.

At the conclusion of the discussion on both topics, Dr. Perlman handed the meeting over to Dr. Paydar who in turn asked Dr. Marks for his Concluding remarks. Dr. Marks thanked the Members of the Committee, the speakers, and Advisory Committee staff. Dr. Paydar then officially adjourned the meeting on January 26, 2023, at 5:30 p.m. EST.

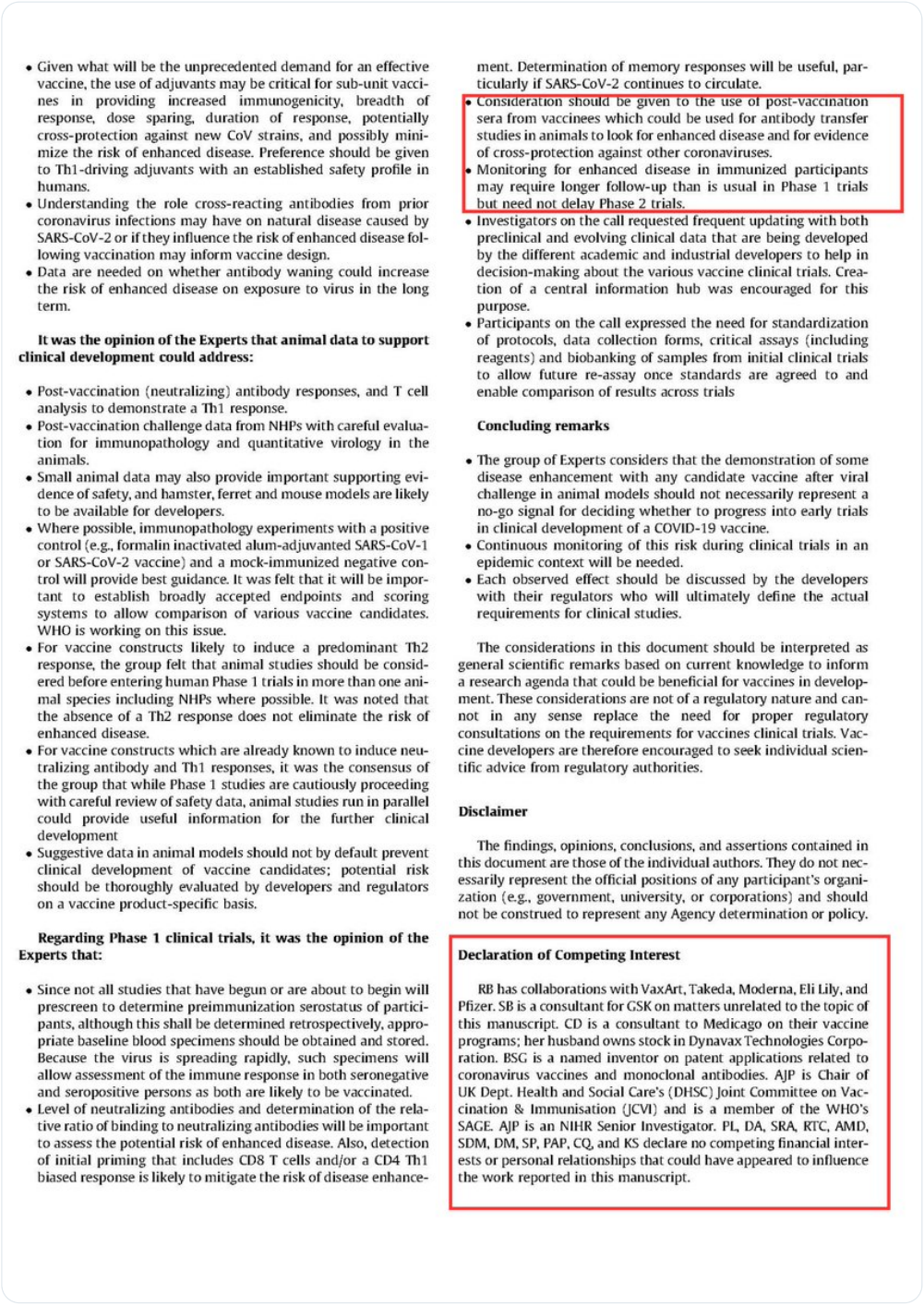
Additional information and details may be obtained from the transcript and the recording of the webcast of the meeting that may be viewed at:

Vaccines and Related Biological Products Advisory Committee January 26, 2023 Meeting Announcement - 01/26/2023 | FDA

10🧵Even more concerning was the funding coming from CEPI & the Brighton Collaboration which is funded by CEPI, the CDC & the Bill & Melinda Gates Foundation. The same Bill gates who took $2bn to invest in C19 jabs for a $200bn ROI. Same CDC that made baseless guidelines.



11🧵The most telling revelation was in the paper's statement of competing interests where it claims that Ralph Baric was in collaborations w/ Eli Lily [maker of monolclonal antibodies], Pfizer, AND Moderna! Where is @RandPaul & the @COVIDSelect on this?!



- Given what will be the unprecedented demand for an effective vaccine, the use of adjuvants may be critical for sub-unit vaccines in providing increased immunogenicity, breadth of response, dose sparing, duration of response, potentially cross-protection against new CoV strains, and possibly minimize the risk of enhanced disease. Preference should be given to Th1-driving adjuvants with an established safety profile in humans.
- Understanding the role cross-reacting antibodies from prior coronavirus infections may have on natural disease caused by SARS-CoV-2 or if they influence the risk of enhanced disease following vaccination may inform vaccine design.
- Data are needed on whether antibody waning could increase the risk of enhanced disease on exposure to virus in the long term.

It was the opinion of the Experts that animal data to support clinical development could address:

- Post-vaccination (neutralizing) antibody responses, and T cell analysis to demonstrate a Th1 response.
- Post-vaccination challenge data from NHPs with careful evaluation for immunopathology and quantitative virology in the animals.
- Small animal data may also provide important supporting evidence of safety, and hamster, ferret and mouse models are likely to be available for developers.
- Where possible, immunopathology experiments with a positive control (e.g., formalin inactivated alum-adjuvanted SARS-CoV-1 or SARS-CoV-2 vaccine) and a mock-immunized negative control will provide best guidance. It was felt that it will be important to establish broadly accepted endpoints and scoring systems to allow comparison of various vaccine candidates. WHO is working on this issue.
- For vaccine constructs likely to induce a predominant Th2 response, the group felt that animal studies should be considered before entering human Phase 1 trials in more than one animal species including NHPs where possible. It was noted that the absence of a Th2 response does not eliminate the risk of enhanced disease.
- For vaccine constructs which are already known to induce neutralizing antibody and Th1 responses, it was the consensus of the group that while Phase 1 studies are cautiously proceeding with careful review of safety data, animal studies run in parallel could provide useful information for the further clinical development
- Suggestive data in animal models should not by default prevent clinical development of vaccine candidates; potential risk should be thoroughly evaluated by developers and regulators on a vaccine product-specific basis.

Regarding Phase 1 clinical trials, it was the opinion of the Experts that:

- Since not all studies that have begun or are about to begin will prescreen to determine preimmunization serostatus of participants, although this shall be determined retrospectively, appropriate baseline blood specimens should be obtained and stored. Because the virus is spreading rapidly, such specimens will allow assessment of the immune response in both seronegative and seropositive persons as both are likely to be vaccinated.
- Level of neutralizing antibodies and determination of the relative ratio of binding to neutralizing antibodies will be important to assess the potential risk of enhanced disease. Also, detection of initial priming that includes CD8 T cells and/or a CD4 Th1 biased response is likely to mitigate the risk of disease enhancement. Determination of memory responses will be useful, particularly if SARS-CoV-2 continues to circulate.
- Consideration should be given to the use of post-vaccination sera from vaccinees which could be used for antibody transfer studies in animals to look for enhanced disease and for evidence of cross-protection against other coronaviruses.
- Monitoring for enhanced disease in immunized participants may require longer follow-up than is usual in Phase 1 trials but need not delay Phase 2 trials.
- Investigators on the call requested frequent updating with both preclinical and evolving clinical data that are being developed by the different academic and industrial developers to help in decision-making about the various vaccine clinical trials. Creation of a central information hub was encouraged for this purpose.
- Participants on the call expressed the need for standardization of protocols, data collection forms, critical assays (including reagents) and biobanking of samples from initial clinical trials to allow future re-assay once standards are agreed to and enable comparison of results across trials

Concluding remarks

- The group of Experts considers that the demonstration of some disease enhancement with any candidate vaccine after viral challenge in animal models should not necessarily represent a no-go signal for deciding whether to progress into early trials in clinical development of a COVID-19 vaccine.
- Continuous monitoring of this risk during clinical trials in an epidemic context will be needed.
- Each observed effect should be discussed by the developers with their regulators who will ultimately define the actual requirements for clinical studies.

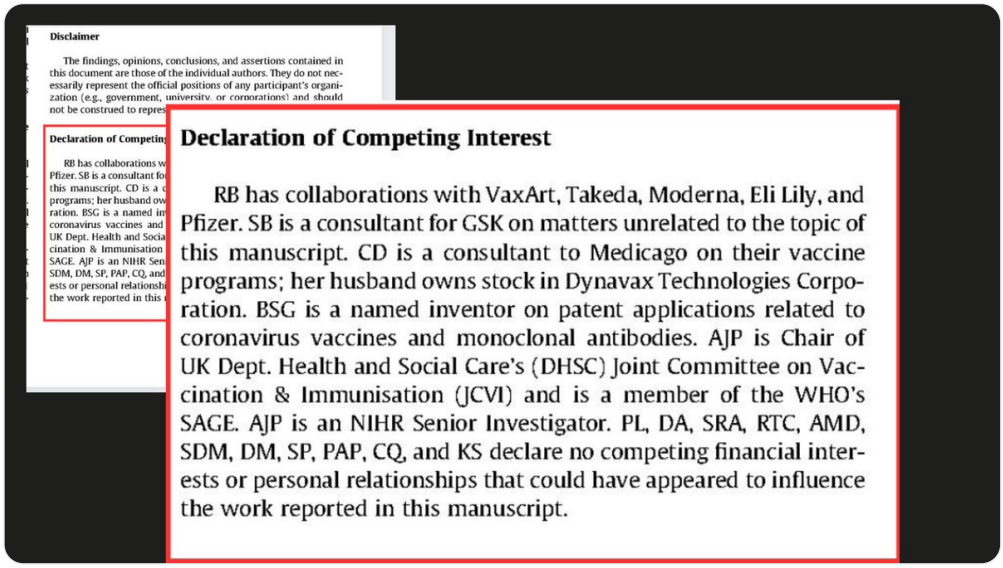
The considerations in this document should be interpreted as general scientific remarks based on current knowledge to inform a research agenda that could be beneficial for vaccines in development. These considerations are not of a regulatory nature and cannot in any sense replace the need for proper regulatory consultations on the requirements for vaccines clinical trials. Vaccine developers are therefore encouraged to seek individual scientific advice from regulatory authorities.

Disclaimer

The findings, opinions, conclusions, and assertions contained in this document are those of the individual authors. They do not necessarily represent the official positions of any participant's organization (e.g., government, university, or corporations) and should not be construed to represent any Agency determination or policy.

Declaration of Competing Interest

RB has collaborations with VaxArt, Takeda, Moderna, Eli Lily, and Pfizer. SB is a consultant for GSK on matters unrelated to the topic of this manuscript. CD is a consultant to Medicago on their vaccine programs; her husband owns stock in Dynavax Technologies Corporation. BSG is a named inventor on patent applications related to coronavirus vaccines and monoclonal antibodies. AJP is Chair of UK Dept. Health and Social Care's (DHSC) Joint Committee on Vaccination & Immunisation (JCVI) and is a member of the WHO's SAGE. AJP is an NIHR Senior Investigator. PL, DA, SRA, RTC, AMD, SDM, DM, SP, PAP, CQ, and KS declare no competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.



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Links: https://pubmed.ncbi.nlm.nih.gov/32507409/

https://en.wikipedia.org/wiki/Brighton_Collaboration

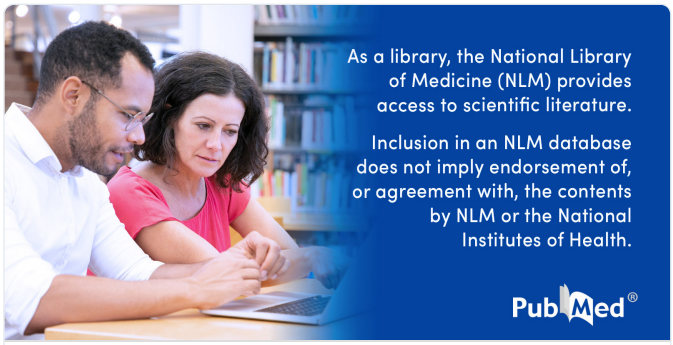
https://news.rice.edu/news/2021/barney-graham-75-named-time-hero-year-developing-covid-19-vaccine

https://www.news-medical.net/news/20201118/Government-funded-scientists-laid-the-groundwork-for-billion-dollar-vaccines.aspx

https://www.nejm.org/doi/full/10.1056/NEJMe2001126

https://www.fda.gov/media/161615/download

@RandPaul @COVIDSelect Paper Link:



Consensus summary report for CEPI/BC March 12-13, 2020 meeting: A…

A novel coronavirus (CoV), Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in late 2019 in Wuhan, China and has since spread as a global pandemic. Safe and effective vaccines ar…

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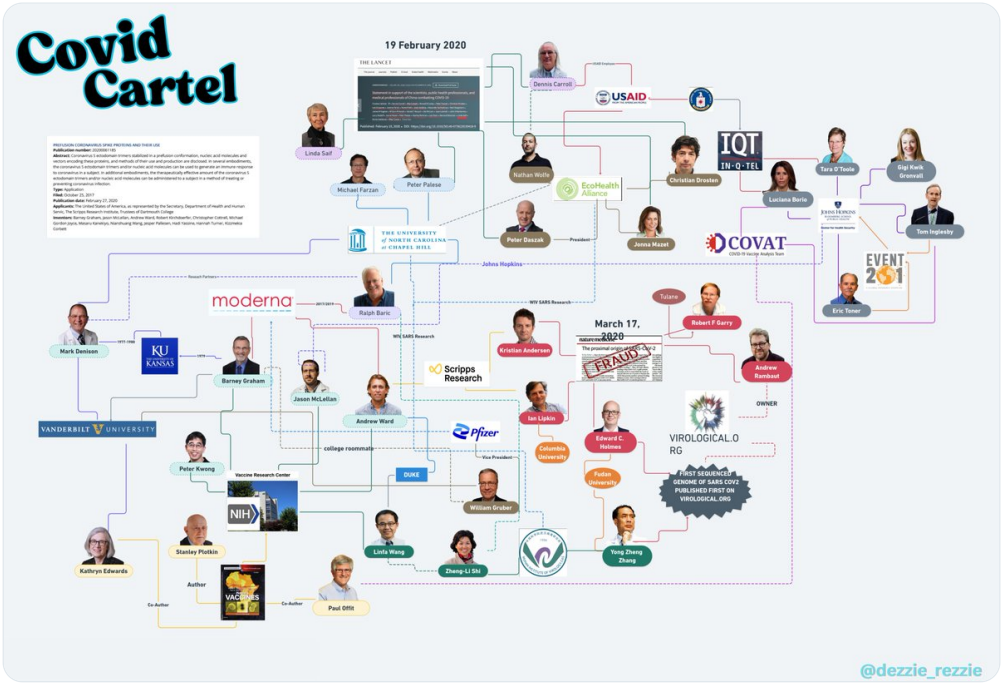
Destiny Rezendes @dezzie_rezzie

Dec 1, 2023 • 12 tweets • dezzie_rezzie/status/1730393042866115023

PART 2 🧵2017 Was a massively important year: VRC+ Moderna collab' on a CoV vaccine, USAID's Andrew Clements emailed EHA staff to move Metabiota from China & instead send EHA, the "PREFUSION CORONAVIRUS SPIKE PROTEINS" patent & a meeting at NIH w/Bill Gates & Graham...



2🧵June 30, 2017 NIH hosts the 4th annual meeting between Bill Gates & the VRC. Attendees included Gates, Graham, Fauci, Collins, and Mascola. The newsletter covering the event shows Graham holding what appears to be the spike protein to show Gates. -Identical to the 2021 one..

NIH RECORD

June 30, 2017
Vol. LXIX, No. 13

National Institutes of Health

ACD Supports Early Investigators, Applauds Collins' Reappointment

BY RICH MCMANUS

Two days before the 114th meeting of the advisory committee to the NIH director on June 8, the President invited NIH director Dr. Francis Collins to remain in that post permanently.

"I am grateful and honored to have received that invitation," said Collins, who had been serving as a holdover appointment since Jan. 18, "and I am happy, along with my wife Diane, to accept it."

The news was met with a round of applause before the ACD got down to a 2-day agenda that included announcement of the Next Generation of Researchers Initiative (NGRI) to support early and mid-career investigators; presentation of NIH's efforts to reduce the nation's opioid epidemic; and an argument for an accelerated pathway toward a universal influenza vaccine.

NIH director Dr. Francis Collins (l), flanked by ACD member Dr. Jose Florez of the Broad Institute of MIT and Harvard, told the group that he thought last December's ACD meeting might have been his last.

Not Ready for Prime Time

Collins traced the half-year history of the effort to reallocate NIH funding for early and mid-career scientists in a more optimum way, starting with what was known last fall as the Research Commitment Index. That effort, known temporarily as RCI, later morphed into the Grant Support Index, or GSI.

"[GSI] created quite a lot of interest—not all of it positive—about as much as I've seen in a grants funding policy in 8 years," said Collins. "We did hear significant concerns about the validity of the index, and how it might discourage collaboration." It became

SEE ACD, PAGE 4

Bill Gates (l) talks global health at NIH, p. 12.

ALSO THIS ISSUE

JUNGLE TRAVEL NOT REQUIRED

Daly Lecturer Describes 21st Century Drug Discovery

BY CARLA GARNETT

Just recently back from a trip to South Africa, where she had a "pretty scary" face-to-face with a deadly black mamba snake, Dr. Fiona Marshall had the perfect introduction to NIH's 2017 Daly lecture.

Renowned jungle explorer Dr. John W. Daly, the late NIDDK biochemist and pharmacologist for whom Marshall's talk was named, pioneered in natural product research.

In much of the last half of last century, he

SEE MARSHALL, PAGE 6

Dr. Fiona Marshall

Genetics, Evolutionary Biology Help Identify Rare Mendelian Disorders

BY DANA TALESNIK

If Charles Darwin had read the findings of Gregor Mendel, he might have saved himself a lot of grief. While Mendel was holed up in a monastery discovering hereditary traits by experimenting on pea plants, Darwin was struggling to prove his theories of natural selection and descent-with-modification.

"Darwin's big problem was that, with descent-with-modification, there was no theory of genetics, no knowledge of

SEE VALLE, PAGE 8

Dr. David Valle

Source:
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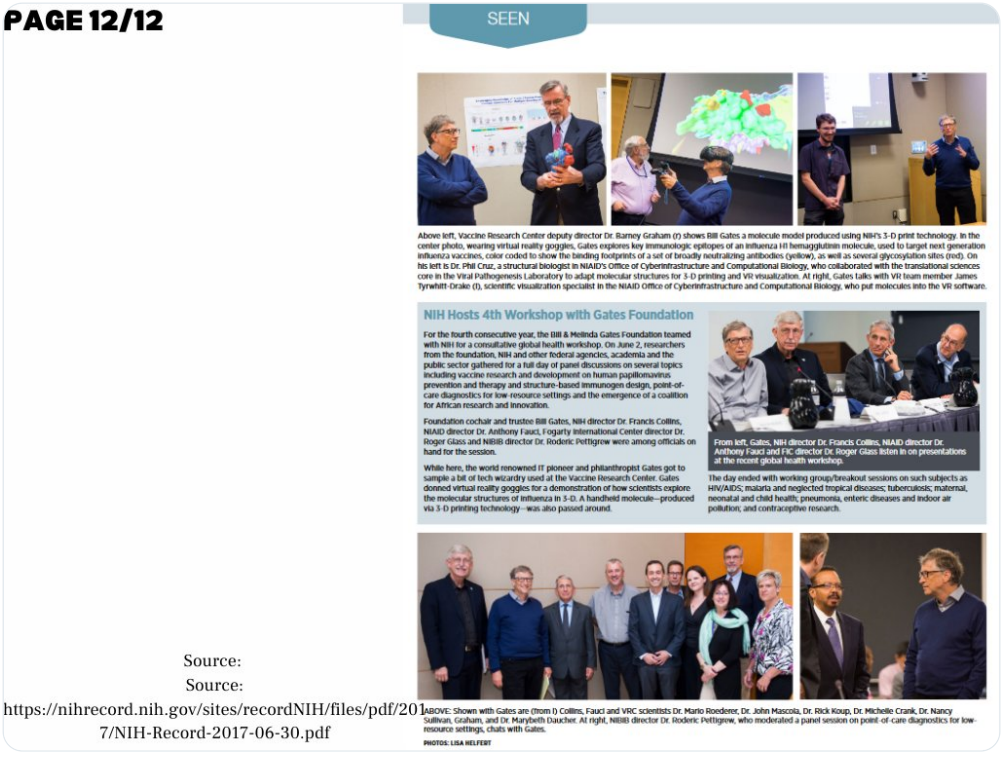
https://nihrecord.nih.gov/sites/recordNIH/files/pdf/201
7/NIH-Record-2017-06-30.pdf



PAGE 12/12

SEEN

Above left, Vaccine Research Center deputy director Dr. Barney Graham (r) shows Bill Gates a molecule model produced using NIH's 3-D print technology. In the center photo, wearing virtual reality goggles, Gates explores key immunologic epitopes of an influenza HI hemagglutinin molecule, used to target next generation influenza vaccines, color coded to show the binding footprints of a set of broadly neutralizing antibodies (yellow), as well as several glycosylation sites (red). On his left is Dr. Phil Cruz, a structural biologist in NIAID's Office of Cyberinfrastructure and Computational Biology, who collaborated with the translational sciences core in the Viral Pathogenesis Laboratory to adapt molecular structures for 3-D printing and VR visualization. At right, Gates talks with VR team member James Tyrwhitt-Drake (l), scientific visualization specialist in the NIAID Office of Cyberinfrastructure and Computational Biology, who put molecules into the VR software.

NIH Hosts 4th Workshop with Gates Foundation

For the fourth consecutive year, the Bill & Melinda Gates Foundation teamed with NIH for a consultative global health workshop. On June 2, researchers from the foundation, NIH and other federal agencies, academia and the public sector gathered for a full day of panel discussions on several topics including vaccine research and development on human papillomavirus prevention and therapy and structure-based immunogen design, point-of-care diagnostics for low-resource settings and the emergence of a coalition for African research and innovation.

Foundation cochair and trustee Bill Gates, NIH director Dr. Francis Collins, NIAID director Dr. Anthony Fauci, Fogarty International Center director Dr. Roger Glass and NIBIB director Dr. Roderic Pettigrew were among officials on hand for the session.

While here, the world renowned IT pioneer and philanthropist Gates got to sample a bit of tech wizardry used at the Vaccine Research Center. Gates donned virtual reality goggles for a demonstration of how scientists explore the molecular structures of influenza in 3-D. A handheld molecule—produced via 3-D printing technology—was also passed around.

From left, Gates, NIH director Dr. Francis Collins, NIAID director Dr. Anthony Fauci and FIC director Dr. Roger Glass listen in on presentations at the recent global health workshop.

The day ended with working group/breakout sessions on such subjects as HIV/AIDS; malaria and neglected tropical diseases; tuberculosis; maternal, neonatal and child health; pneumonia, enteric diseases and indoor air pollution; and contraceptive research.

ABOVE: Shown with Gates are (from l) Collins, Fauci and VRC scientists Dr. Mario Roederer, Dr. John Mascola, Dr. Rick Koup, Dr. Michelle Crank, Dr. Nancy Sullivan, Graham, and Dr. Marybeth Daucher. At right, NIBIB director Dr. Roderic Pettigrew, who moderated a panel session on point-of-care diagnostics for low-resource settings, chats with Gates.

PHOTOS: LISA HELFERT

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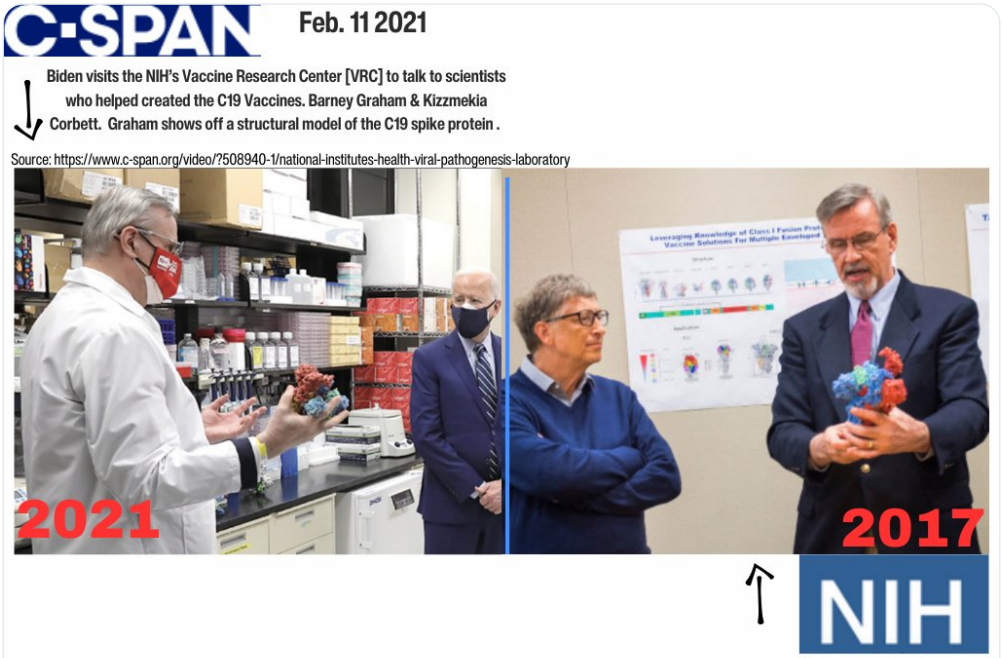
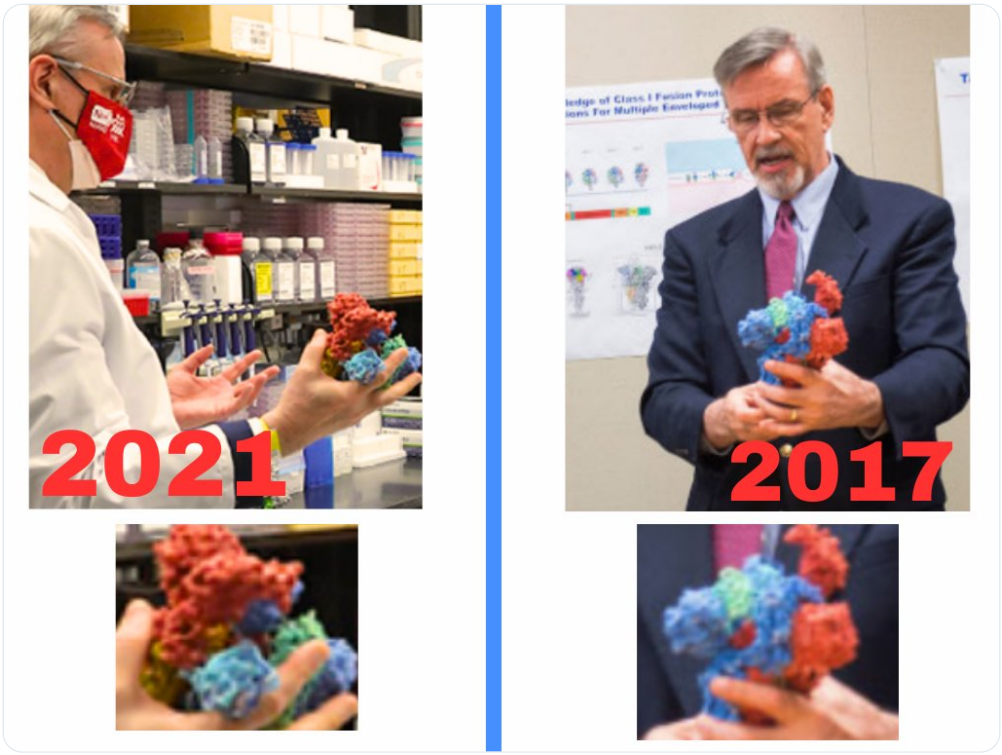
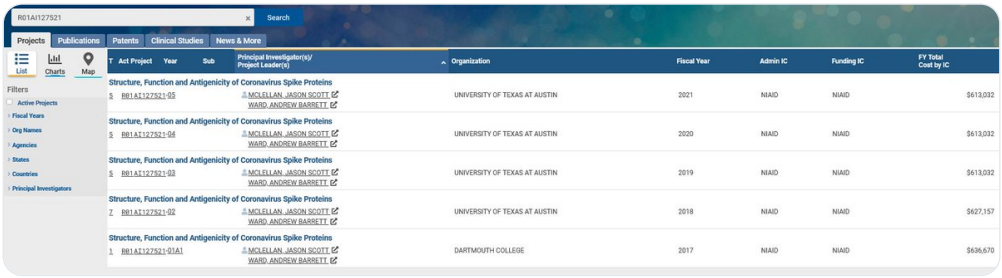
https://nihrecord.nih.gov/sites/recordNIH/files/pdf/201
7/NIH-Record-2017-06-30.pdf



Bill Gates & Barney Graham in 2017 for the annual meeting between Gate and NIH/NIAID/HHS,



3🧵On Feb 09 2017 The NIH began a grant round titled: "Structure, Function & Antigenicity of Coronavirus Spike Proteins" led by McLellan & Ward out of Dartmouth. The grant # is R01AI127521 & went 5 grant cycles from 2017-2021.



Agency	National Institute of Health (NIH)	**Project Start**	2017-02-09
Institute	National Institute of Allergy and Infectious Diseases (NIAID)	**Project End**	2022-01-31
		Budget Start	2017-02-09
Type	Research Project (R01)	**Budget End**	2018-01-31
Project #	1R01AI127521-01A1	**Support Year**	1
Application #	9328799	**Fiscal Year**	2017
Study Section	Virology - A Study Section (VIRA)	**Total Cost**	$636,670
		Indirect Cost	$124,349
Program Officer	Stemmy, Erik J		

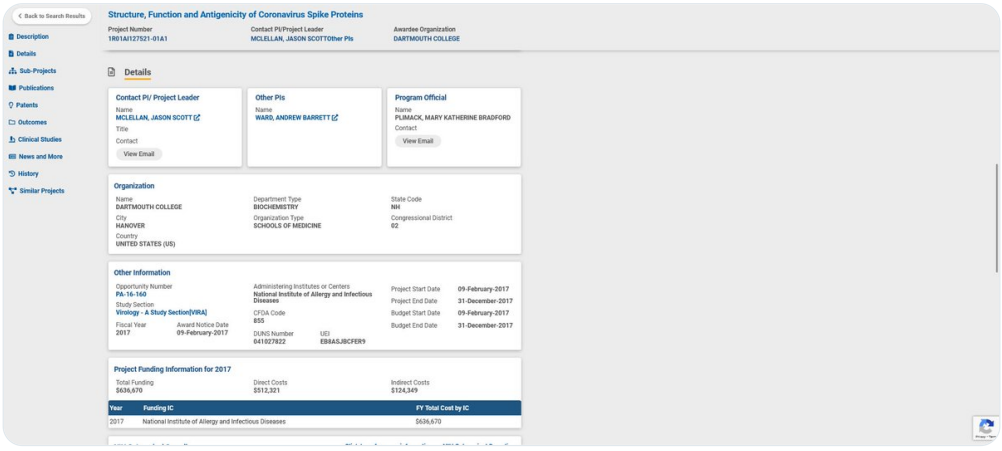
Institution

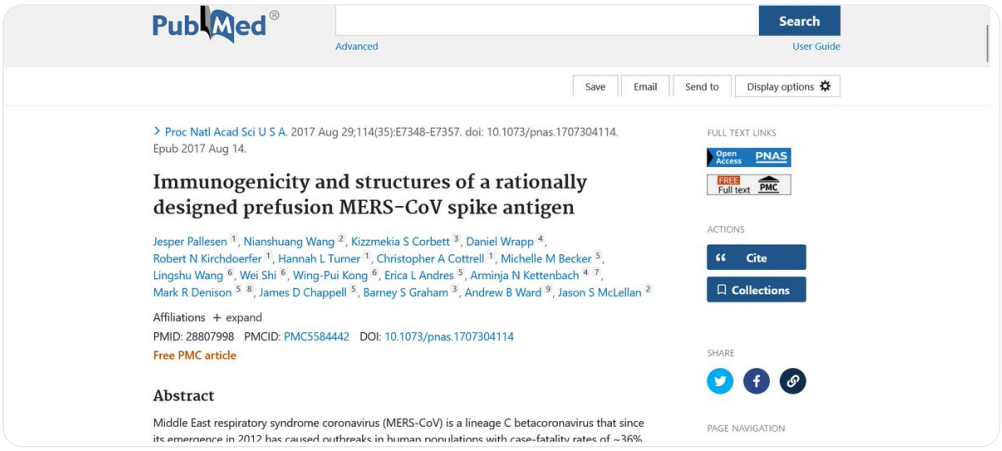
Name	Dartmouth College	**City**	Hanover
Department	Biochemistry	**State**	NH
Type	Schools of Medicine	**Country**	United States
DUNS #	041027822	**Zip Code**	03755

NIH 2021 R01 AI	Structure, Function and Antigenicity of Coronavirus Spike Proteins McLellan, Jason Scott; Ward, Andrew Barrett / University of Texas Austin	
NIH 2020 R01 AI	Structure, Function and Antigenicity of Coronavirus Spike Proteins McLellan, Jason Scott; Ward, Andrew Barrett / University of Texas Austin	
NIH 2019 R01 AI	Structure, Function and Antigenicity of Coronavirus Spike Proteins McLellan, Jason Scott; Ward, Andrew Barrett / University of Texas Austin	
NIH 2018 R01 AI	Structure, Function and Antigenicity of Coronavirus Spike Proteins McLellan, Jason Scott; Ward, Andrew Barrett / University of Texas Austin	
NIH 2017 R01 AI	Structure, Function and Antigenicity of Coronavirus Spike Proteins McLellan, Jason Scott; Ward, Andrew Barrett / Dartmouth College	$636,670

Yes, both Doctors Jason McLellan and Andrew Ward are associated with Dartmouth College. Jason McLellan is a professor of molecular biosciences at The University of Texas in Austin, and his lab is located at Dartmouth College in New Hampshire [3]. Andrew Ward is also linked to Dartmouth College, as a collaboration between Jason McLellan's group at Dartmouth and Andrew Ward's group took place in 2017, just three years before the emergence of SARS-CoV-2 [5].

4🧵W/in the NIH grant rounds under R01AI127521 a publication was funded. That paper, "Immunogenicity & structures of a rationally designed prefusion MERS-CoV spike antigen" was authored by not only Graham, Ward + McLellan but also Corbett & Denison👀





Agency	National Institute of Health (NIH)	**Project Start**	2017-02-09
Institute	National Institute of Allergy and Infectious Diseases (NIAID)	**Project End**	2022-01-31
		Budget Start	2017-02-09
Type	Research Project (R01)	**Budget End**	2018-01-31
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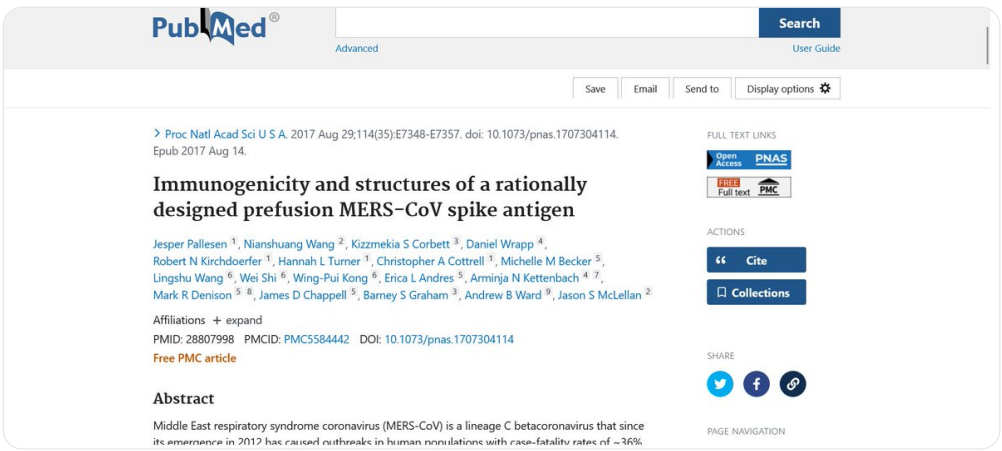
NIH 2019 R01 AI	Structure, Function and Antigenicity of Coronavirus Spike Proteins McLellan, Jason Scott; Ward, Andrew Barrett / University of Texas Austin	
NIH 2018 R01 AI	Structure, Function and Antigenicity of Coronavirus Spike Proteins McLellan, Jason Scott; Ward, Andrew Barrett / University of Texas Austin	
NIH 2017 R01 AI	Structure, Function and Antigenicity of Coronavirus Spike Proteins McLellan, Jason Scott; Ward, Andrew Barrett / Dartmouth College	$636,670

5🧵Corbett was the young black female scientist at the VRC in that 2021 video w/ Biden & Graham. She happens to be an understudy of Ralph Baric, graduate of UNC Chapel Hill. Denison was the top collab of Baric's during 2014-2020 from Vanderbilt.



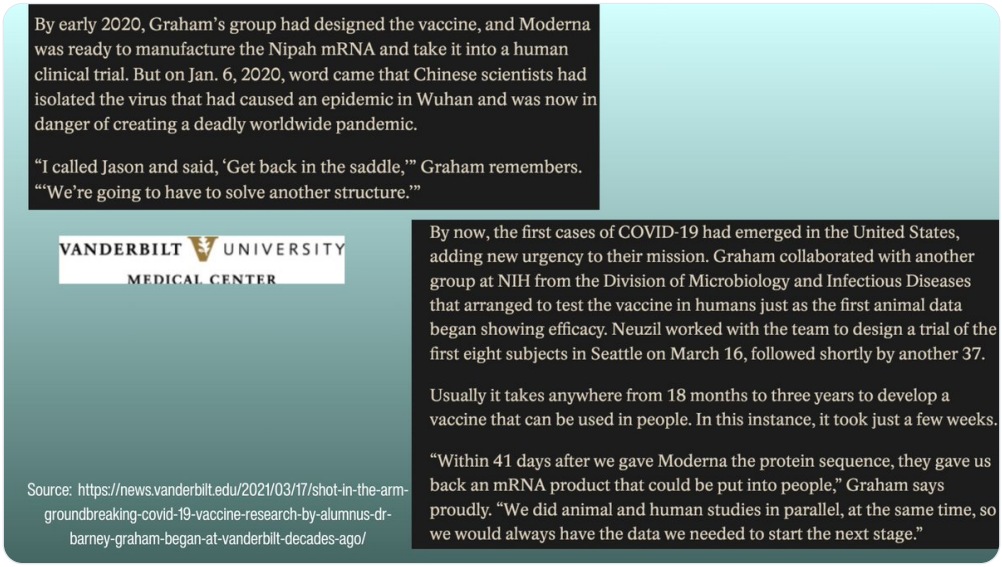
VANDERBILT UNIVERSITY MEDICAL CENTER

Source: https://news.vanderbilt.edu/2021/03/17/shot-in-the-arm-groundbreaking-covid-19-vaccine-research-by-alumnus-dr-barney-graham-began-at-vanderbilt-decades-ago/

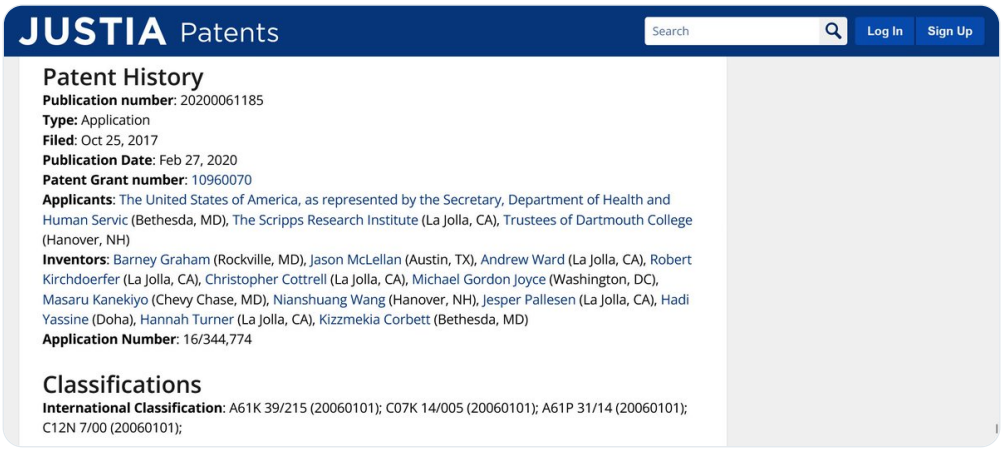
CORONAVIRUS BREAKTHROUGH

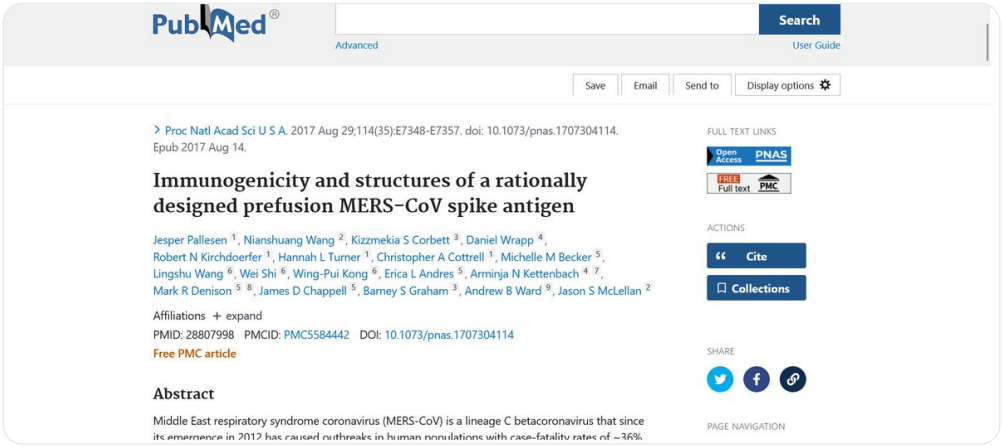
Wright, Graham, Neuzil and Denison formed the nucleus of a unique community, which also included Dr. Kathryn Edwards and Dr. Bill Gruber. Edwards is now the Sarah H. Sell and Cornelius Vanderbilt Professor of Pediatrics at the School of Medicine. Gruber, who had been Graham's roommate at Rice and had come to Vanderbilt to work on vaccine trials for several viral diseases affecting children, is now the senior vice president of vaccine clinical research and development at Pfizer.

The group was unusually collaborative—Graham and Neuzil were adult physicians working on a childhood disease, while Wright, Edwards and Gruber were pediatricians running trials on an adult vaccine. Graham became the bridge among the various disciplines of adult and childhood diseases, as well as the basic science and clinical research.



6🧵Two months after the "...prefusion MERS-CoV spike antigen" article a patent was issued on Oct 25 2017 titled: "PREFUSION CORONAVIRUS SPIKE PROTEINS AND THEIR USE" credited to HHS, Scripps and Dartmouth w/ Ward, McLellan, Graham & Corbett. This patent is credited 4 the C19 💉





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> Proc Natl Acad Sci U S A. 2017 Aug 29;114(35):E7348-E7357. doi: 10.1073/pnas.1707304114. Epub 2017 Aug 14.

Immunogenicity and structures of a rationally designed prefusion MERS-CoV spike antigen

Jesper Pallesen [1], Nianshuang Wang [2], Kizzmekia S Corbett [3], Daniel Wrapp [4], Robert N Kirchdoerfer [1], Hannah L Turner [1], Christopher A Cottrell [1], Michelle M Becker [5], Lingshu Wang [6], Wei Shi [6], Wing-Pui Kong [6], Erica L Andres [5], Arminja N Kettenbach [4 7], Mark R Denison [5 8], James D Chappell [5], Barney S Graham [3], Andrew B Ward [9], Jason S McLellan [2]

Affiliations + expand

PMID: 28807998 PMCID: PMC5584442 DOI: 10.1073/pnas.1707304114

Free PMC article

Abstract

Middle East respiratory syndrome coronavirus (MERS-CoV) is a lineage C betacoronavirus that since its emergence in 2012 has caused outbreaks in human populations with case-fatality rates of ~36%

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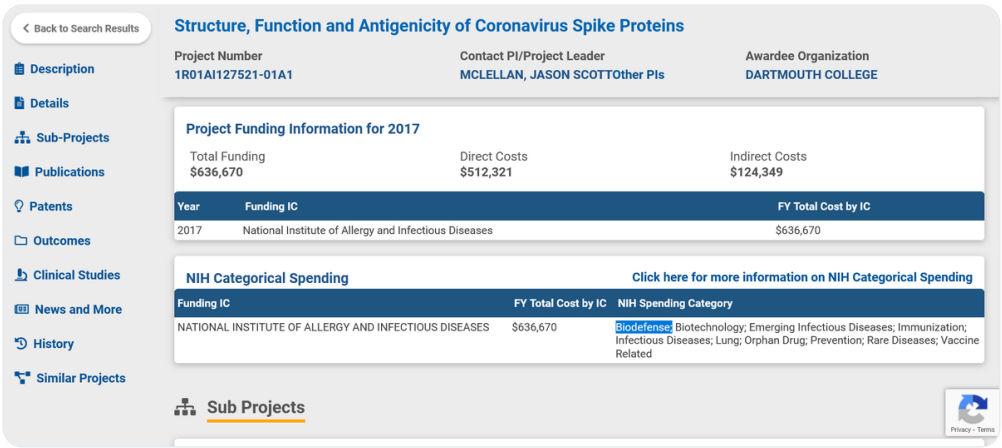
PREFUSION CORONAVIRUS SPIKE PROTEINS AND THEIR USE

Oct 25, 2017 - The United States of America, as represented by the Secretary, Department of Health and Human Servic

Coronavirus S ectodomain trimers stabilized in a prefusion conformation, nucleic acid molecules and vectors encoding these proteins, and methods of their use and production are disclosed. In several embodiments, the coronavirus S ectodomain trimers and/or nucleic acid molecules can be used to generate an immune response to coronavirus in a subject. In additional embodiments, the therapeutically effective amount of the coronavirus S ectodomain trimers and/or nucleic acid molecules can be administered to a subject in a method of treating or preventing coronavirus infection.

7🧵Two things that surprised me was; #1 the classification of the research under grant R01AI127521 which according to the NIH's grant repository RePORTER was listed as "Biodefense"



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Structure, Function and Antigenicity of Coronavirus Spike Proteins

Project Number	Contact PI/Project Leader	Awardee Organization
1R01AI127521-01A1	MCLELLAN, JASON SCOTTOther PIs	DARTMOUTH COLLEGE

Project Funding Information for 2017

Total Funding	Direct Costs	Indirect Costs
$636,670	$512,321	$124,349

Year	Funding IC	FY Total Cost by IC
2017	National Institute of Allergy and Infectious Diseases	$636,670

NIH Categorical Spending Click here for more information on NIH Categorical Spending

Funding IC	FY Total Cost by IC	NIH Spending Category
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$636,670	Biodefense; Biotechnology; Emerging Infectious Diseases; Immunization; Infectious Diseases; Lung; Orphan Drug; Prevention; Rare Diseases; Vaccine Related

Sub Projects

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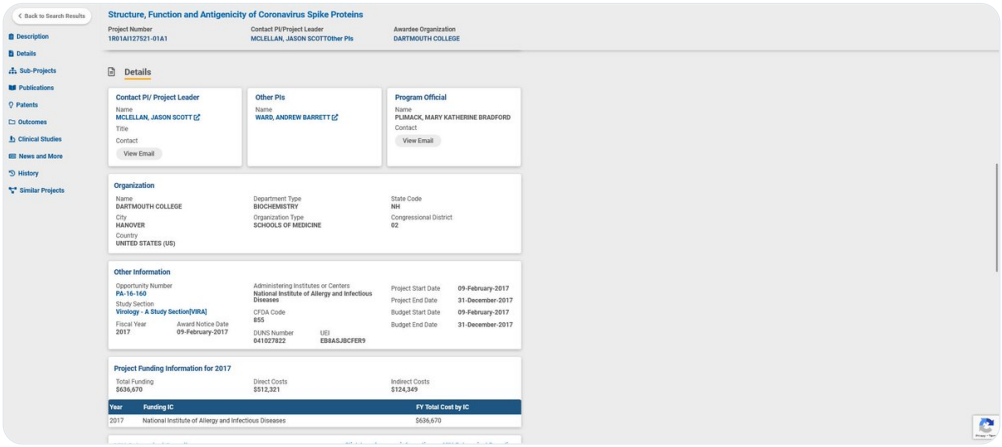
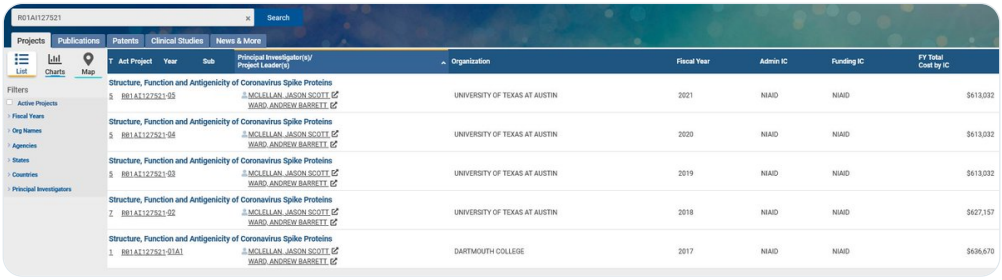
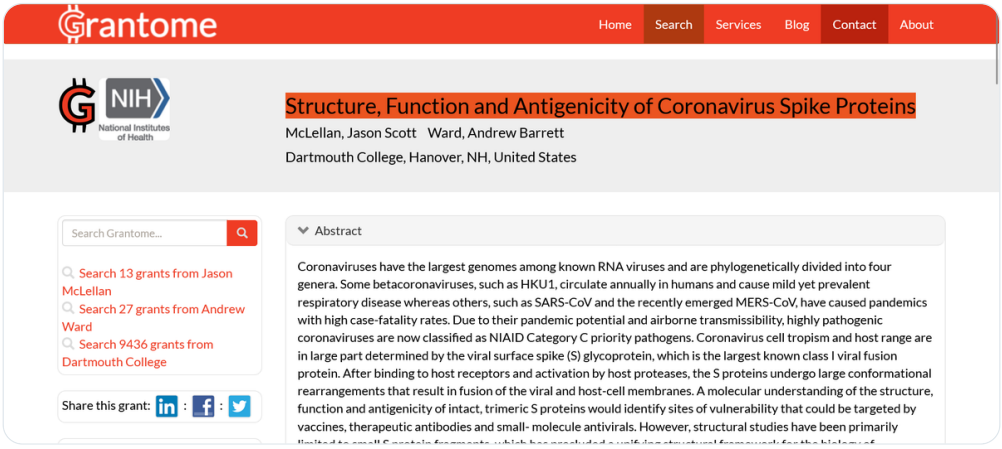
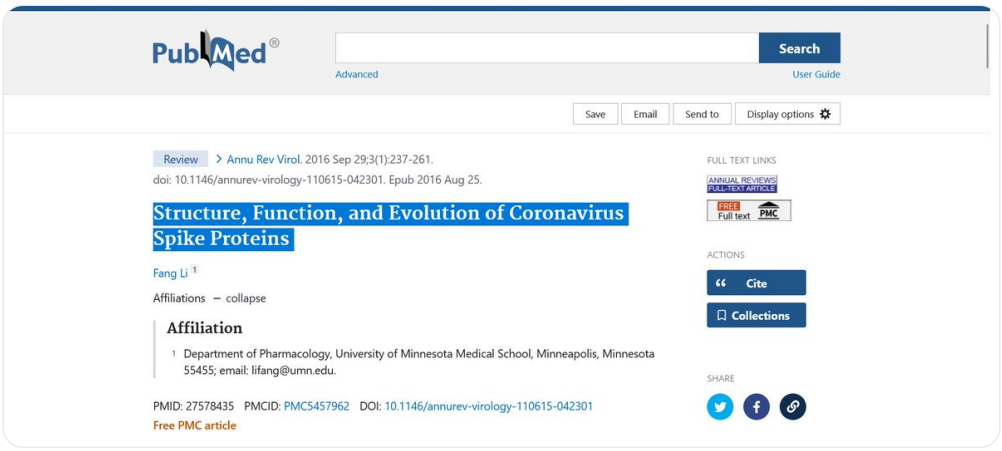


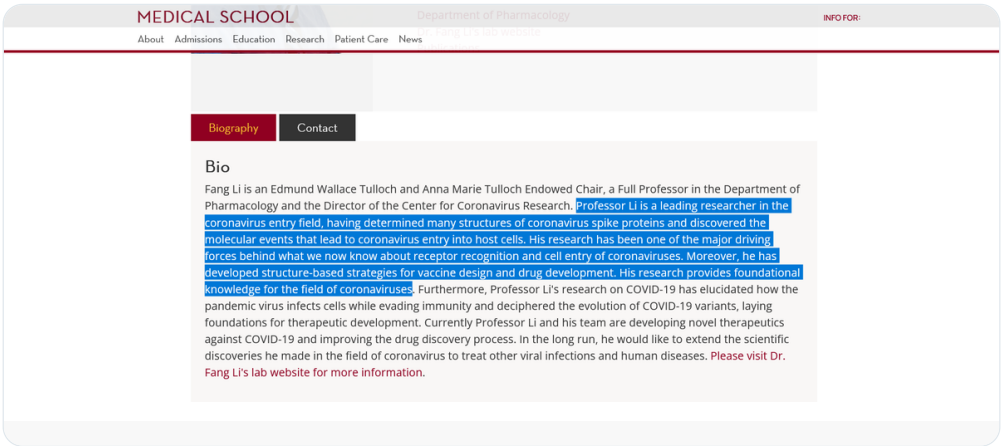


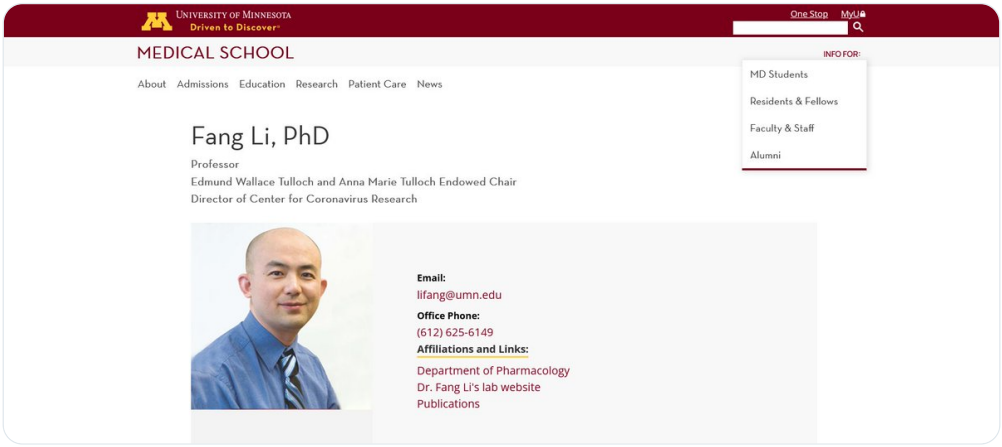
8🧵#2- If you were to type the 2017 grant title "Structure, Function & Antigenicity of Coronavirus Spike Proteins" into NIH's Pubmed you get a paper titled "Structure, Function, and Evolution of Coronavirus Spike Proteins" from Sept 29 2016. The titles are one word off...





9🧵One word off but NONE of the same Authors. The 2016 paper is written solely by Fang-Li of Univ. Minn. The paper isn't even funded by the same grant [R01AI127521] but it is funded by grants AI110700, & AI089728. Both grants are to Fang-Li for CoV research.





Review > Annu Rev Virol. 2016 Sep 29;3(1):237-261.
doi: 10.1146/annurev-virology-110615-042301. Epub 2016 Aug 25.

Structure, Function, and Evolution of Coronavirus Spike Proteins

Fang Li [1]

Affiliations – collapse

Affiliation

1 Department of Pharmacology, University of Minnesota Medical School, Minneapolis, Minnesota 55455; email: lifang@umn.edu.

PMID: 27578435 PMCID: PMC5457962 DOI: 10.1146/annurev-virology-110615-042301
Free PMC article

Substances

> Membrane Glycoproteins
> Receptors, Virus
> Spike Glycoprotein, Coronavirus
> Viral Envelope Proteins

Related information

Domains
MedGen
PMC images

Grants and funding

R01 AI089728/AI/NIAID NIH HHS/United States
R01 AI110700/AI/NIAID NIH HHS/United States

10 🧵 One of those NIH grants [AI110700] was co-led by none other than Ralph Baric. Again, same titled research, which led to the patent for C19 💉's but hidden under different grants,

even though the 💉patent is used by Moderna which Baric already signed an MTA w/ <1yr later 🤔

Review > Annu Rev Virol. 2016 Sep 29;3(1):237-261.
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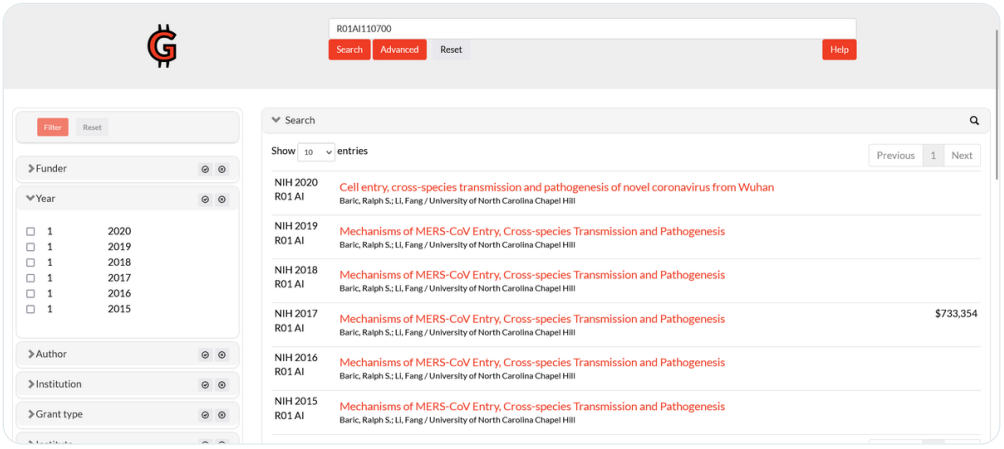

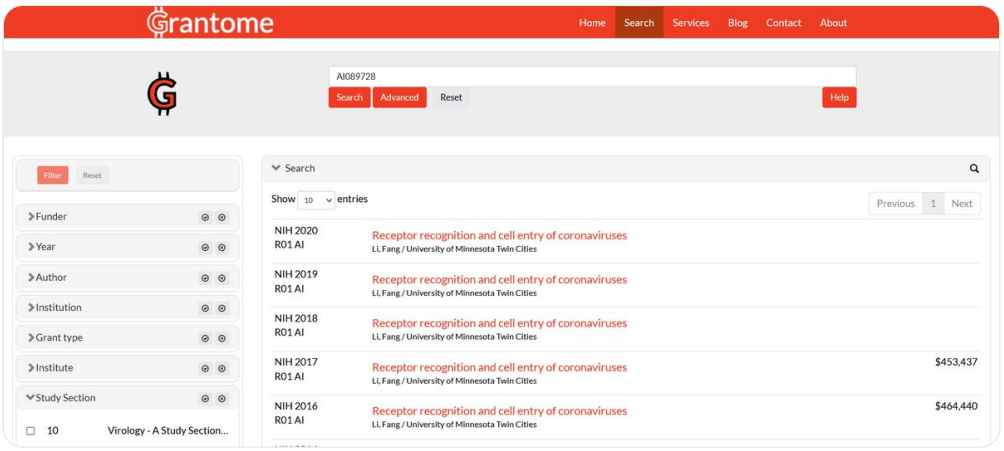

11🧵If Fang-Li sounds familiar it's likely because he has worked significantly with Baric & Zheng-Li Shi & Eco Health Alliance on Coronaviruses & now is the Director, Center for Coronavirus Research😳

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GENETIC DIVERSITY AND EVOLUTION

Discovery of Novel Bat Coronaviruses in South China That Use the Same Receptor as Middle East Respiratory Syndrome Coronavirus

Chu-Ming Luo,[a,b,c] Ning Wang,[a,b] Xing-Lou Yang,[a] Hai-Zhou Liu,[a] Wei Zhang,[a] Bei Li,[a] Ben Hu,[a] Cheng Peng,[a] Qi-Bin Geng,[c] Guang-Jian Zhu,[d] Fang Li,[c] Zheng-Li Shi[a]

[a]CAS Key Laboratory of Special Pathogens and Biosafety, Wuhan Institute of Virology, Chinese Academy of Sciences, Wuhan, Hubei, China
[b]University of Chinese Academy of Sciences, Beijing, China
[c]Department of Veterinary and Biomedical Sciences, University of Minnesota, Saint Paul, Minnesota, USA
[d]EcoHealth Alliance, New York, New York, USA

ABSTRACT Middle East respiratory syndrome coronavirus (MERS-CoV) has represented a human health threat since 2012. Although several MERS-related CoVs that

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[a]CAS Key Laboratory of Special Pathogens and Biosafety, Wuhan Institute of Virology, Chinese Academy of Sciences, Wuhan, Hubei, China
[b]University of Chinese Academy of Sciences, Beijing, China
[c]Department of Veterinary and Biomedical Sciences, University of Minnesota, Saint Paul, Minnesota, USA
[d]EcoHealth Alliance, New York, New York, USA

ABSTRACT Middle East respiratory syndrome coronavirus (MERS-CoV) has represented a human health threat since 2012. Although several MERS-related CoVs that belong to the same species as MERS-CoV have been identified from bats, they do not use the MERS-CoV receptor, dipeptidyl peptidase 4 (DPP4). Here, we screened 1,059 bat samples from at least 30 bat species collected in different regions in south China and identified 89 strains of lineage C betacoronaviruses, including *Tylonycteris pachypus coronavirus HKU4*, *Pipistrellus pipistrellus coronavirus HKU5*, and MERS-related CoVs. We sequenced the full-length genomes of two positive samples collected from the great evening bat, *Ia io*, from Guangdong Province. The two genomes were highly similar and exhibited genomic structures identical to those of other lineage C betacoronaviruses. While they exhibited genome-wide nucleotide identities of only 75.3 to 81.2% with other MERS-related CoVs, their gene-coding regions were highly similar to their counterparts, except in the case of the spike proteins. Further protein-protein interaction assays demonstrated that the spike proteins of these MERS-related CoVs bind to the receptor DPP4. Recombination analysis suggested that the newly discovered MERS-related CoVs have acquired their spike genes from a DPP4-recognizing bat coronavirus HKU4. Our study provides further evidence that bats represent the evolutionary origins of MERS-CoV.

IMPORTANCE Previous studies suggested that MERS-CoV originated in bats. However, its evolutionary path from bats to humans remains unclear. In this study, we discovered 89 novel lineage C betacoronaviruses in eight bat species. We provide evidence of a MERS-related CoV derived from the great evening bat that uses the same host receptor as human MERS-CoV. This virus also provides evidence for a natural recombination event between the bat MERS-related CoV and another bat coronavirus, HKU4. Our study expands the host ranges of MERS-related CoV and represents an important step toward establishing bats as the natural reservoir of MERS-CoV. These findings may lead to improved epidemiological surveillance of MERS-CoV and the prevention and control of the spread of MERS-CoV to humans.

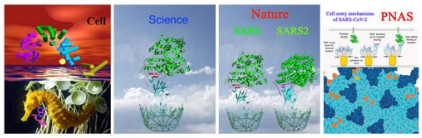
KEYWORDS MERS-related coronavirus, bat, dipeptidyl peptidase 4, virus discovery

Coronaviruses (CoVs) infect a wide range of mammalian and avian hosts, causing respiratory, enteric, hepatic, or neurological diseases of varying severity. These viruses have the largest genomes among all RNA viruses, leading to an increased number of replication errors compared to the host genome (1). Different CoVs can also recombine their genomes upon infecting the same host cell, contributing substantially

Received 22 January 2018 **Accepted** 3 April 2018
Accepted manuscript posted online 18 April 2018
Citation Luo C, Wang N, Yang X, Liu H, Zhang W, Li B, Hu B, Peng C, Geng Q, Zhu G, Li F, Shi Z. 2018. Discovery of novel bat coronaviruses in South China that use the same receptor as Middle East respiratory syndrome coronavirus. J Virol 92:e00116-18. https://doi.org/10.1128/JVI.00116-18.
Editor Tom Gallagher, Loyola University Medical Center

Address correspondence to Fang Li, lifang@umn.edu, or Zheng-Li Shi, zlshi@wh.iov.cn.

Laboratory of Structural Biology of Disease



Resume, Research, Publications, Awards, News, CCR

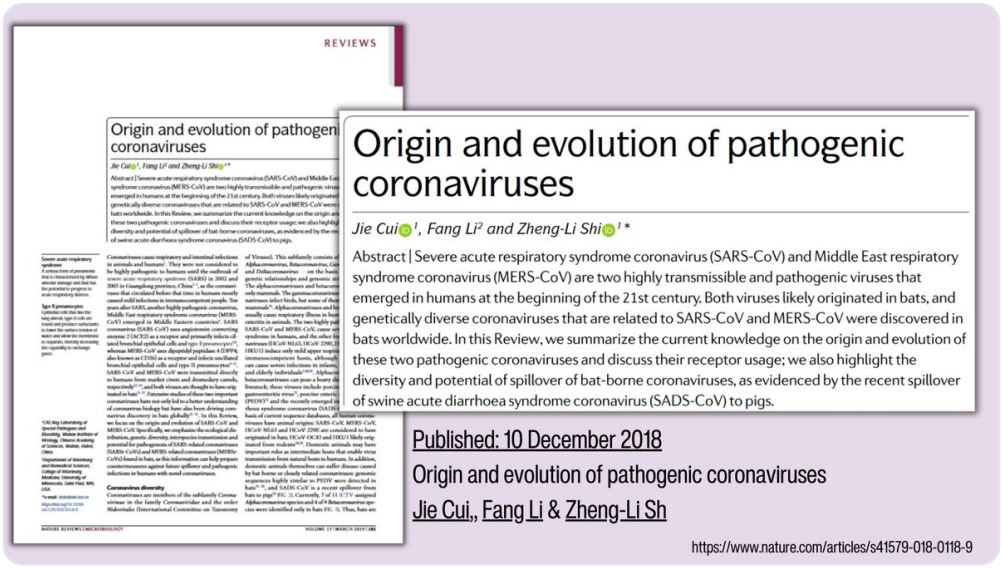
Fang Li, PhD

Professor and Endowed Chair, Deparment of Pharmacology

Director, Center for Coronavirus Research

Co-Director, Midwest Antiviral Drug Discovery Center

University of Minnesota Medical School



12🧵Coincidence? I think not. An attempt to hide the creation of certain GoF research turned bio-weapon? MUCH more likely. Stay tuned-I'm still not done 🔎👀🧾

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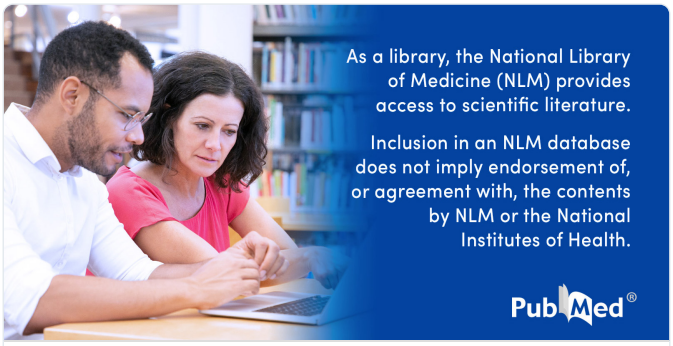

Structure, Function, and Evolution of Coronavirus Spike Proteins - Pu…
The coronavirus spike protein is a multifunctional molecular machine that mediates coronavirus entry into host cells. It first binds to a receptor on the host cell surface through its S1 subunit and …

https://pubmed.ncbi.nlm.nih.gov/27578435/

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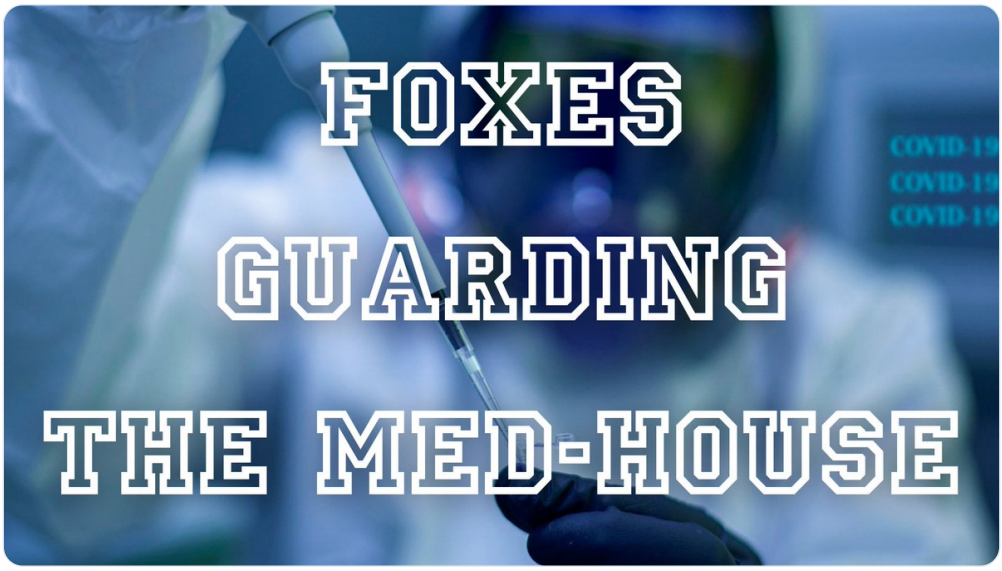
• • •

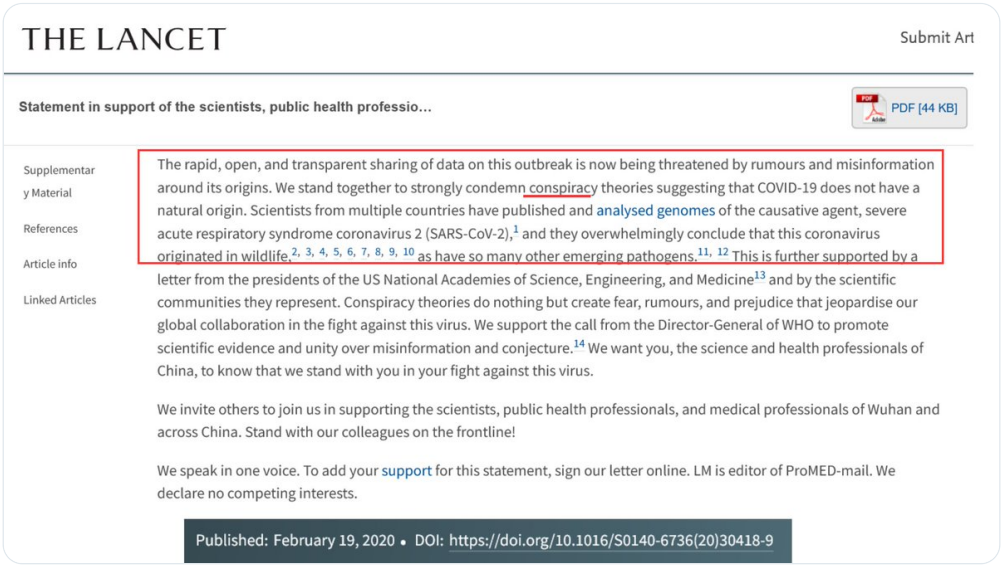
Destiny Rezendes @dezzie_rezzie

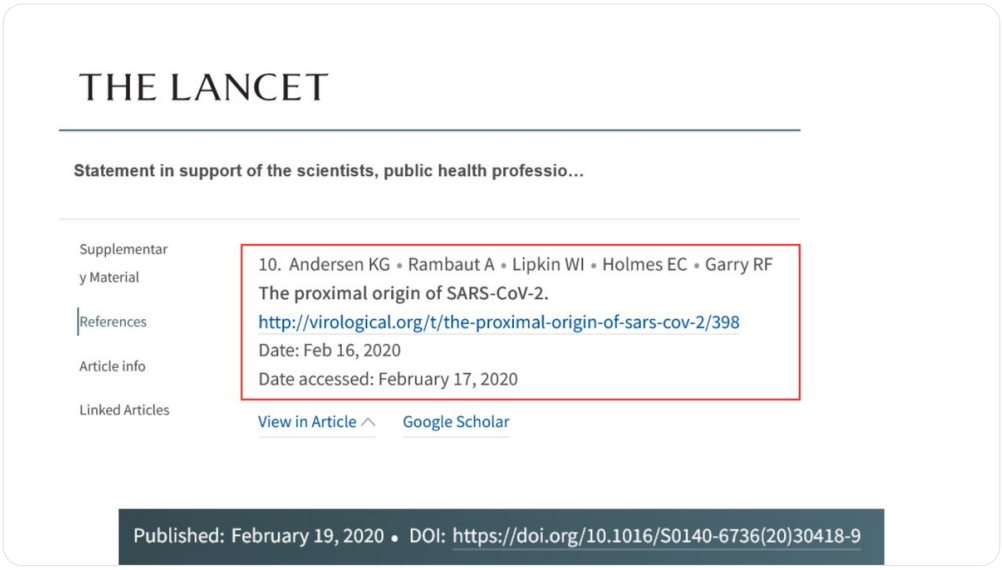
Dec 2, 2023 • 13 tweets • dezzie_rezzie/status/1731093081661772169

1🧵Continuing w/ my recent threads exposing the Conflicts of Interest [COI] in the oversight efforts & early investigations of the pandemic. I have more data to prove to you that this 'Scamdemic' is a certified rigged racket.



2🧵40 days after the C19 genome was made public a group of "concerned" scientists submitted a statement to stand in support of "the science" in Wuhan. Admonishing the "conspiracy theories" floating around of a lab leak. Published in the lancet, it is a certified fraud.





3🧵The paper was signed by a slew of implicated characters; Dennis Carroll [ex USAID] & he is joined by fellow EHA heads Karesh, Mazet, Field, & Daszak. NIH cronies like Palese, Turner & Perlman. The Wellcome Trust poster child Jeremy Farrar & virologist Linda Saif 🤫

of 2019 novel coronavirus disease (COVID-19) and are deeply concerned about its impact on global health and wellbeing. We have watched as the scientists, public health professionals, and medical professionals of China, in particular, have worked diligently and effectively to rapidly identify the pathogen behind this outbreak, put in place significant measures to reduce its impact, and share their results transparently with the global health community. This effort has been remarkable.

We sign this statement in solidarity with all scientists and health professionals in China who continue to save lives and protect global health during the challenge of the COVID-19 outbreak. We are all in this together, with our Chinese counterparts in the forefront, against this new viral threat.

The rapid, open, and transparent

We invite others to join us in supporting the scientists, public health professionals, and medical professionals of Wuhan and across China. Stand with our colleagues on the frontline!

We speak in one voice. To add your support for this statement, sign our letter online. LM is editor of ProMED-mail. We declare no competing interests.

Charles Calisher, Dennis Carroll, Rita Colwell, Ronald B Corley, Peter Daszak, Christian Drosten, Luis Enjuanes, Jeremy Farrar, Hume Field, Josie Golding, Alexander Gorbalenya, Bart Haagmans, James M Hughes, William B Karesh, Gerald T Keusch, Sai Kit Lam, Juan Lubroth, John S Mackenzie, Larry Madoff, Jonna Mazet, Peter Palese, Stanley Perlman, Leo Poon, Bernard Roizman, Linda Saif, Kanta Subbarao, Mike Turner

COVID19statement@gmail.com

The rapid, open, and transparent sharing of data on this outbreak is now being threatened by rumours and misinformation around its origins. We stand together to strongly condemn conspiracy theories suggesting that COVID-19 does not have a natural origin. Scientists from multiple countries have published and analysed genomes of the causative agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[1] and they overwhelmingly conclude that this coronavirus originated in wildlife,[2-10] as have so many other emerging pathogens.[11,12] This is further supported by a letter from the presidents of the US National Academies of Science, Engineering, and Medicine[13] and by the scientific communities they represent. Conspiracy theories do

Correspondence

Statement in support of the scientists, public health professionals, and medical professionals of China combatting COVID-19

We are public health scientists who have closely followed the emergence of 2019 novel coronavirus disease (COVID-19) and are deeply concerned about its impact on global health and wellbeing. We have watched as the scientists, public health professionals, and medical professionals of China, in particular, have worked diligently and effectively to rapidly identify the pathogen behind this outbreak, put in place significant measures to reduce its impact, and share their results transparently with the global health community. This effort has been remarkable.

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We invite others to join us in supporting the scientists, public health professionals, and medical professionals of Wuhan and across China. Stand with our colleagues on the frontline!

We speak in one voice. To add your support for this statement, sign our letter online. I M is editor of ProMED-mail. We declare no competing interests.

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COVID19statement@gmail.com

Colorado State University, Fort Collins, CO, USA (CC); Scowcroft Institute of International Affairs, Texas A&M, College Station, TX, USA (DC); University of Maryland, College Park, MD, USA (RC); NEIDL Institute (RBC), Boston University (GTIC), Boston, MA, USA; EcoHealth Alliance, New York, NY, USA (PD); Charité – Universitatsmedizin Berlin, Berlin, Germany (CD); National Center of Biotechnology, Madrid, Spain (LE); The Wellcome Trust, London, UK (JF, JG, MT); School of Veterinary Science, The University of Queensland, Brisbane, QLD, Australia (HF); Leiden University Medical Center, Leiden, Netherlands (AG); Erasmus Medical Center, Rotterdam, Netherlands (BH); Emory University, Atlanta, GA, USA (JMH); World Organization for Animal Health (OIE) Working Group on Wildlife, New York, NY, USA (WIBC); University of Malaya, Kuala Lumpur, Malaysia (SKL); Food and Agriculture Organization of the United Nations, Rome, Italy (JL); Curtin University, Perth, WA, Australia (JSMi); Massachusetts Medical School, Worcester, MA, USA (LM); University of California at Davis, Davis, CA, USA (JM); Department of Microbiology, Icahn School of Medicine, Mt Sinai Hospital, New York, NY, USA (PP); University of Iowa, Roy J and Lucille A Carver College of Medicine, Iowa City, IA, USA (SP); The University of Hong Kong, Hong Kong (LP), University of Chicago, Chigaco, IL, USA (BR); The Ohio State University, Columbus, OH, USA (LS); and The University of Melbourne, Melbourne, VIC, Australia (KS)

1 Gorbalenya AE, Baker SC, Baric RS, et al. Severe acute respiratory syndrome-related coronavirus: the species and its viruses—a statement of the Coronavirus Study Group. *bioRxiv* 2020; published online Feb 11. DOI:2020.02.07.937862 (preprint).

2 Zhou P, Yang X-L, Wang X-G, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020; published online Feb 3. DOI:10.1038/s41586-020-2012-7.

3 Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020; published online Jan 30. https://doi.org/10.1016/S0140-6736(20)30251-8.

4 Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *NEJM* 2020; published online Jan 24. DOI:10.1056/NEJMoa2001017.

5 Ren L, Wang Y-M, Wu Z-Q, et al. Identification of a novel coronavirus causing severe pneumonia in humans: a descriptive study. *Chin Med J* 2020; published online Feb 11. DOI:10.1097/CM9.0000000000000722.

6 Paraskevis D, Kostaki EG, Magiorkinis G, Panayiotakopoulos G, Tsiodras S. Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. *Infect Genet Evol* 2020; published online Jan 29. DOI:10.1016/j.meegid.2020.104212.

7 Benvenuto D, Giovanetti M, Ciccozzi A, Spoto S, Angeletti S, Ciccozzi M. The 2019-new coronavirus epidemic: evidence for virus evolution. *J Med Virol* 2020; published online Jan 29. DOI:10.1002/jmv.25688.

8 Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. *J Virol* 2020; published online Jan 29. DOI:10.1128/JVI.00127-20.

9 US Center for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19) situation summary. Feb 16, 2020. https://www.cdc.gov/coronavirus/2019-nCoV/summary.html (accessed Feb 8, 2020).

10 Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The proximal origin of SARS-CoV-2. Feb 16, 2020. http://virological.org/t/the-proximal-origin-of-sars-cov-2/398 (accessed Feb 17, 2020).

11 Bengis R, Leighton F, Fischer J, Artois M, Morner T, Tate C. The role of wildlife in emerging and re-emerging zoonoses. *Rev Sci Tech* 2004; 23: 497–511.

12 Woolhouse ME, Gowtage-Sequeria S. Host range and emerging and reemerging pathogens. *Emerg Infect Dis* 2005; 11: 1842–47.

13 NASEM. The National Academies of Science Engineering and Medicine of the USA. NAS, NAE, and NAM presidents' letter to the White House Office of Science and Technology Policy. Feb 6, 2020. https://www.nationalacademies.org/includes/NASEMs%20Responses%20to%20OSTPs%20re%20Coronavirus_February%206,%202020.pdf (accessed Feb 7, 2020).

Published Online February 18, 2020 https://doi.org/10.1016/S0140-6736(20)30418-9

For the Chinese translation see Online for appendix

To register your support see http://chng.it/5DpTBy8T

For the SARS-CoV-2 genome analysis see https://www.gisaid.org/epiflu-applications/next-betacov-app/

Submissions should be made via our electronic submission system at http://ees.elsevier.com/thelancet/

4🧵The paper uses the CIA-Warren Commission Era tactic of tossing around the label of "conspiracy theorist" to ostracize those against the corrupt narrative. Ralph Baric is the first reference they cited & the Proximal Origins paper & WE are the conspiracy theorists?! 👀

Hong Kong, Hong Kong (LP); University of Chicago, Chigaco, IL, USA (BR); The Ohio State University, Columbus, OH, USA (LS); and The University of Melbourne, Melboune, VIC, Australia (KS)

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11 Bengis R, Leighton F, Fischer J, Artois M, Morner T, Tate C. The role of wildlife in emerging and re-emerging zoonoses. *Rev Sci Tech* 2004; **23:** 497–512.

12 Woolhouse ME, Gowtage-Sequeria S. Host range and emerging and reemerging pathogens. *Emerg Infect Dis* 2005; **11:** 1842–47.

13 NASEM. The National Academies of Science Engineering and Medicine of the USA. NAS, NAE, and NAM presidents' letter to the White House Office of Science and Technology Policy. Feb 6, 2020. https://www.nationalacademies.org/includes/NASEM%20Response%20to%20OSTP%20re%20Coronavirus_February%206,%202020.pdf (accessed Feb 7, 2020).

For the **SARS-CoV-2 genome analysis** see https://www.gisaid.org/epiflu-applications/next-betacov-app/

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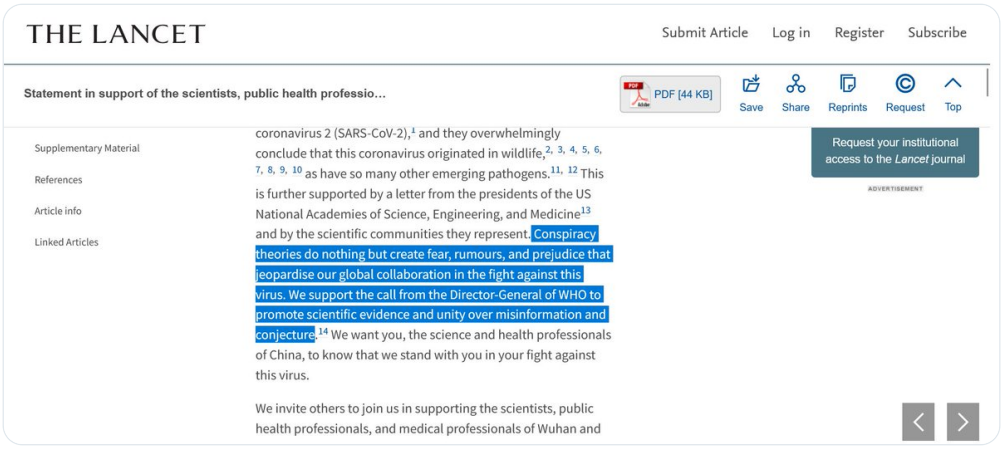


5🧵To me, Linda Saif is the red flag in the authors listed. A NAS Ohio State virologist who assisted the WHO during the 2003 SARS outbreak was a familiar name from FOIA'd emails between Baric, Daszak & Fauci from early on in 2020.

February 12, 2020

From: Su, Lishan <lishan_su@med.unc.edu>
Sent: Wednesday, February 12, 2020 1:12 AM
To: Baric, Ralph S <rbaric@email.unc.edu>
Subject: A commentary on 2019 nCoV vs lab engineered viruses

Hi Ralph:

In response to the EMI journal editor's request, Drs. Shan-Lu Liu, Lin Saif and myself are writing a commentary (1-2 pages) to dispute the rumors of 2019 nCoV origin. Will you be interested, and have time, to have a quick read/comment? Please let me know if you have time.

Tentative Title: Is 2019-nCoV laboratory origin?

Thanks!

-Lishan

February 12, 2020

From: Saif, Linda
To: Liu, Shan-Lu; lishan_su@med.unc.edu
Subject: FW: A commentary on 2019 nCoV vs lab engineered viruses
Date: Wednesday, February 12, 2020 1:28:39 PM
Attachments: EMI-2019-nCoV_Commentary LJS_SLL_Refs-rsb.docx

Hi
Please note that Ralph made these changes on an earlier copy sent to him so hopefully the 2 of you can incorporate them into the updated draft I sent this AM!
Regards,
Linda

Linda J. Saif, PhD
Distinguished University Professor
Food Animal Health Research Program
OARDC/The Ohio State University
1680 Madison Ave
Wooster, Oh 44691

February 12, 2020

From: Su, Lishan <lishan_su@med.unc.edu>
Sent: Wednesday, February 12, 2020 10:11 AM
To: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: A commentary on 2019 nCoV vs lab engineered viruses

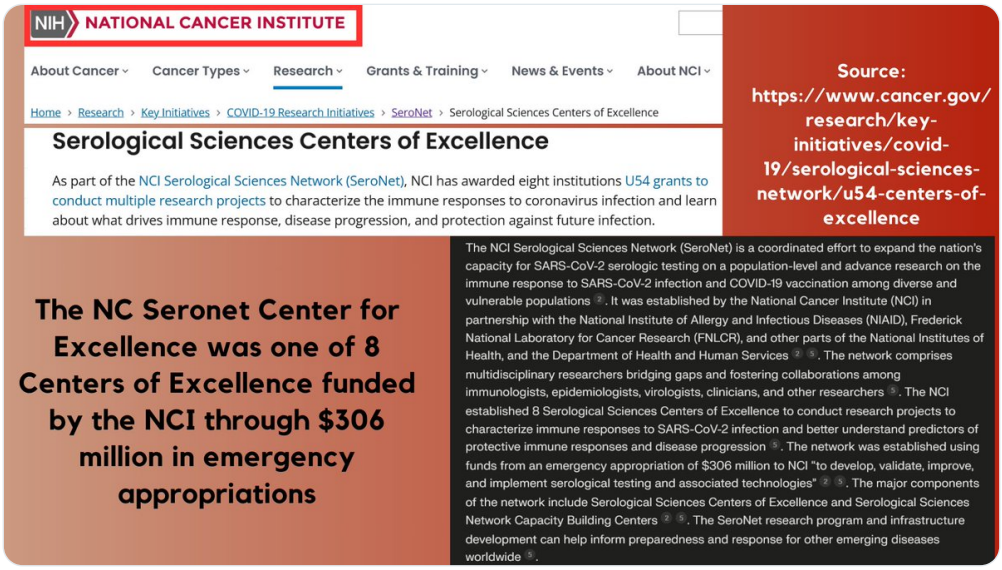
Hi Ralph:
We are trying to finish it and had no plan to get you too involved, but I do value your input. It is almost final and we are also getting comments from Perlman and Weiss.
Thanks,

-Lishan

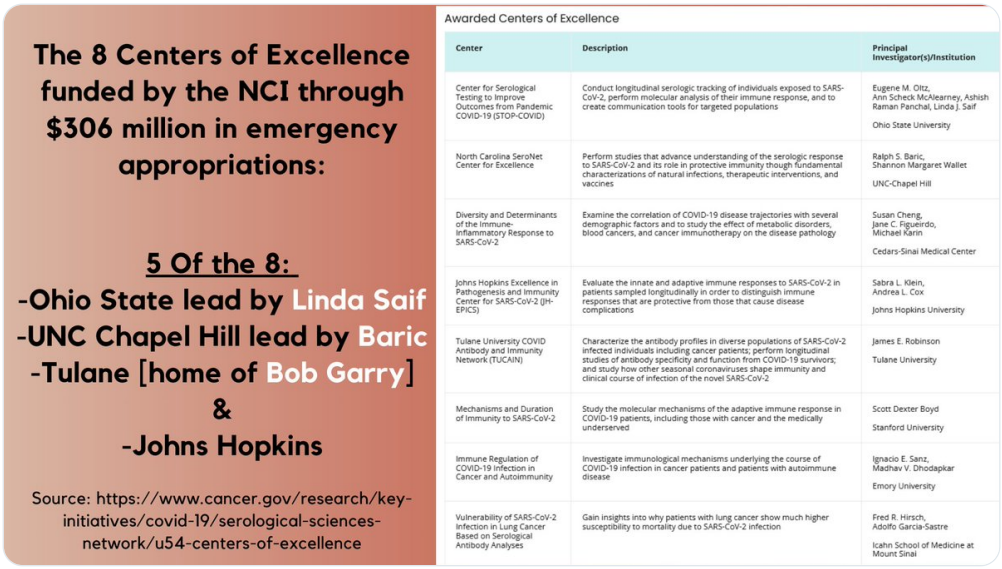
From: "Baric, Ralph S" <rbaric@email.unc.edu>
Date: Wednesday, February 12, 2020 at 10:02 AM
To: "Su, Lishan" <lishan_su@med.unc.edu>
Subject: RE: A commentary on 2019 nCoV vs lab engineered viruses

sure, but don't want to be cited in as having commented prior to submission.

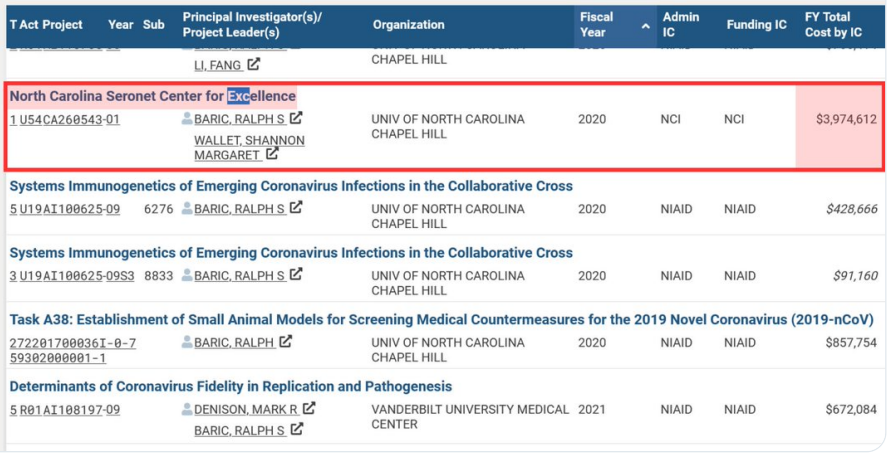
6🧵The emails show Saif and her co-workers emailing Baric about the paper in support of the Wuhan research. Why was she so concerned? I think I know why. While researching Baric's grants I found one for the NC Seronet Center for Excellence [NCSCE] Turns out the NCSCE is new!



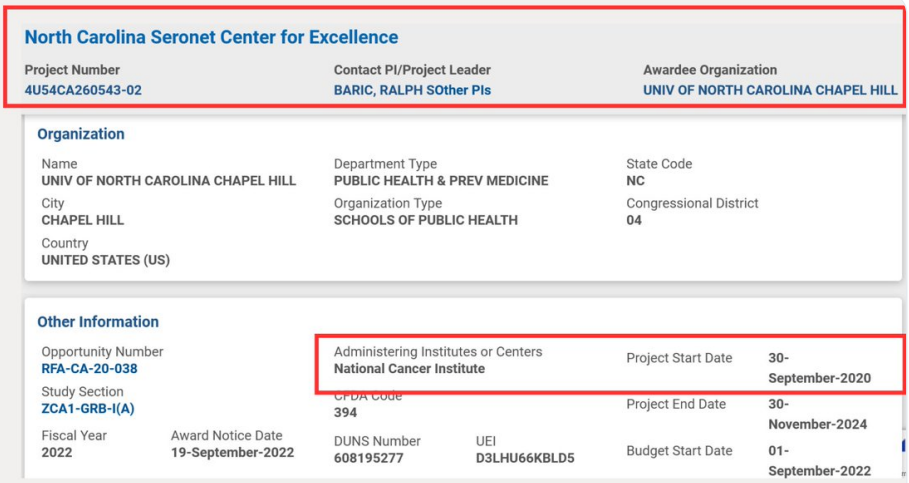
7🧵The NCSCE is one of 8 "Centers of Excellence" established w/a $306M fund- not by NIAID, but rather the National Cancer Institute even though the focus is on C19.🤔 Of the lucky 8 Centers created, Linda Saif of Ohio State was a recipient of a center just like Baric.💰😳



Also in 2020, Baric receives a grant through the North Carolina Seronet Center for Excellence but its not funded by NIH/NIAID but rather by the National Cancer Institute for $3.9 Million dollars



T Act Project	Year	Sub	Principal Investigator(s)/ Project Leader(s)	Organization	Fiscal Year	Admin IC	Funding IC	FY Total Cost by IC
			LI, FANG	CHAPEL HILL				
North Carolina Seronet Center for Excellence								
1 U54CA260543-01			BARIC, RALPH S WALLET, SHANNON MARGARET	UNIV OF NORTH CAROLINA CHAPEL HILL	2020	NCI	NCI	$3,974,612
Systems Immunogenetics of Emerging Coronavirus Infections in the Collaborative Cross								
5 U19AI100625-09		6276	BARIC, RALPH S	UNIV OF NORTH CAROLINA CHAPEL HILL	2020	NIAID	NIAID	*$428,666*
Systems Immunogenetics of Emerging Coronavirus Infections in the Collaborative Cross								
3 U19AI100625-09S3		8833	BARIC, RALPH S	UNIV OF NORTH CAROLINA CHAPEL HILL	2020	NIAID	NIAID	*$91,160*
Task A38: Establishment of Small Animal Models for Screening Medical Countermeasures for the 2019 Novel Coronavirus (2019-nCoV)								
272201700036I-0-7 59302000001-1			BARIC, RALPH	UNIV OF NORTH CAROLINA CHAPEL HILL	2020	NIAID	NIAID	$857,754
Determinants of Coronavirus Fidelity in Replication and Pathogenesis								
5 R01AI108197-09			DENISON, MARK R BARIC, RALPH S	VANDERBILT UNIVERSITY MEDICAL CENTER	2021	NIAID	NIAID	$672,084



North Carolina Seronet Center for Excellence

Project Number	Contact PI/Project Leader	Awardee Organization
4U54CA260543-02	BARIC, RALPH SOther PIs	UNIV OF NORTH CAROLINA CHAPEL HILL

Organization

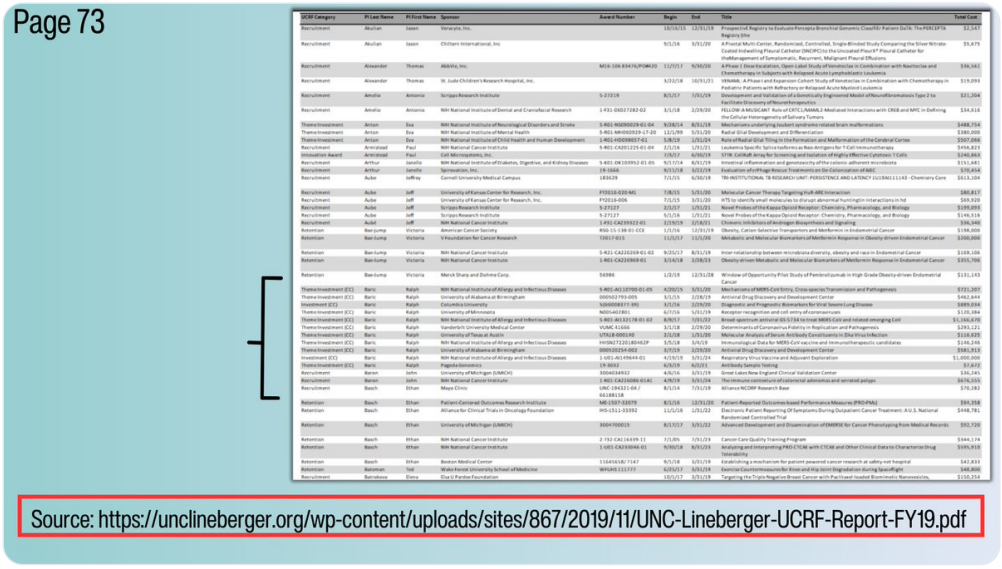
Name UNIV OF NORTH CAROLINA CHAPEL HILL	Department Type PUBLIC HEALTH & PREV MEDICINE	State Code NC
City CHAPEL HILL	Organization Type SCHOOLS OF PUBLIC HEALTH	Congressional District 04
Country UNITED STATES (US)		

Other Information

Opportunity Number RFA-CA-20-038		Administering Institutes or Centers National Cancer Institute	Project Start Date	30-September-2020
Study Section ZCA1-GRB-I(A)		CFDA Code 394	Project End Date	30-November-2024
Fiscal Year 2022	Award Notice Date 19-September-2022	DUNS Number 608195277	UEI D3LHU66KBLD5	Budget Start Date 01-September-2022

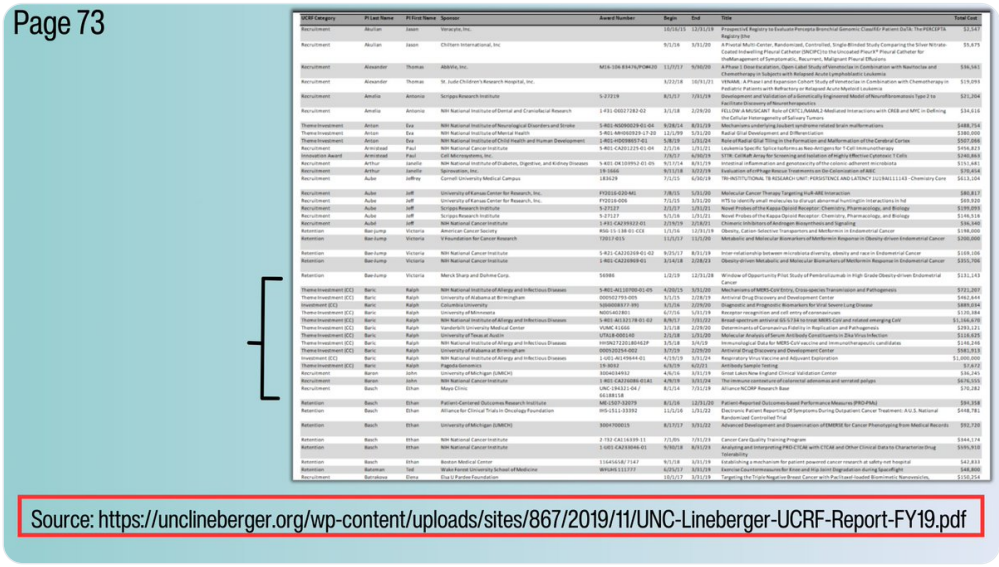
8🧵Are you surprised by the funding being from NCI? I wasn't & only because I found that since 2019 more & more funds are going to Baric and not through NIH as much, but through the NCI. I have proof of this in UNC's Lineberger Cancer Institute's funding report for 2019...

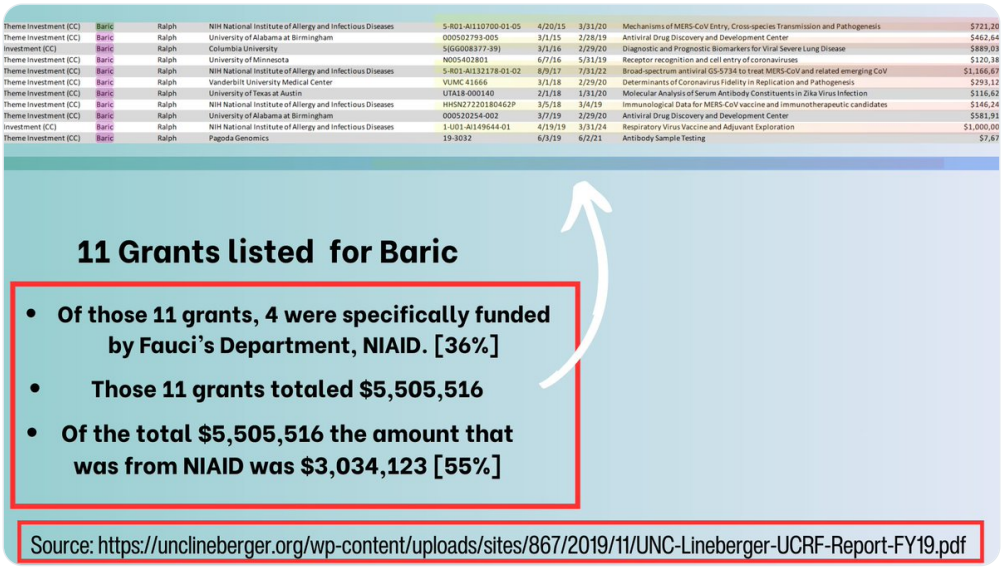
Source: https://unclineberger.org/wp-content/uploads/sites/867/2019/11/UNC-Lineberger-UCRF-Report-FY19.pdf



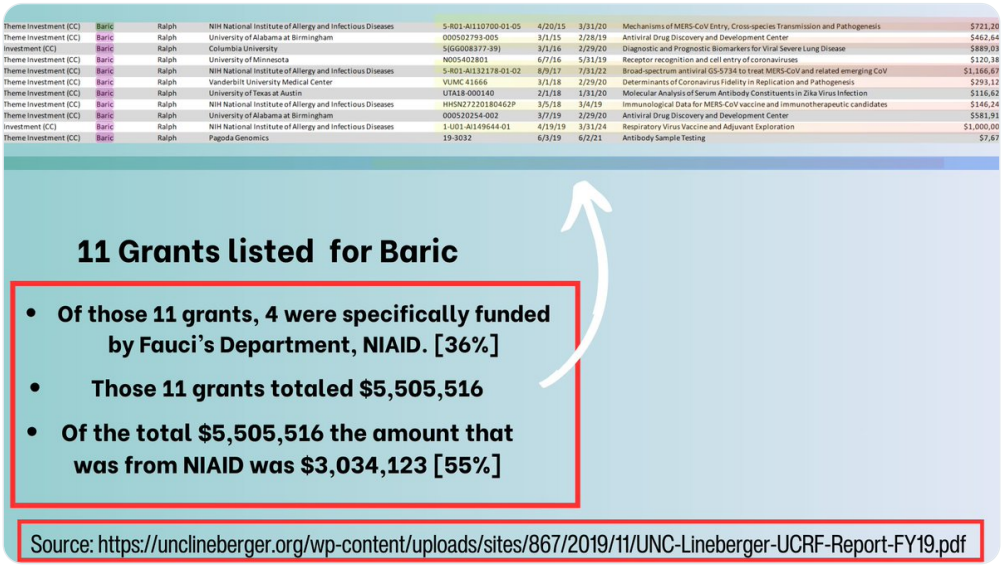
Source: https://unclineberger.org/wp-content/uploads/sites/867/2019/11/UNC-Lineberger-UCRF-Report-FY19.pdf

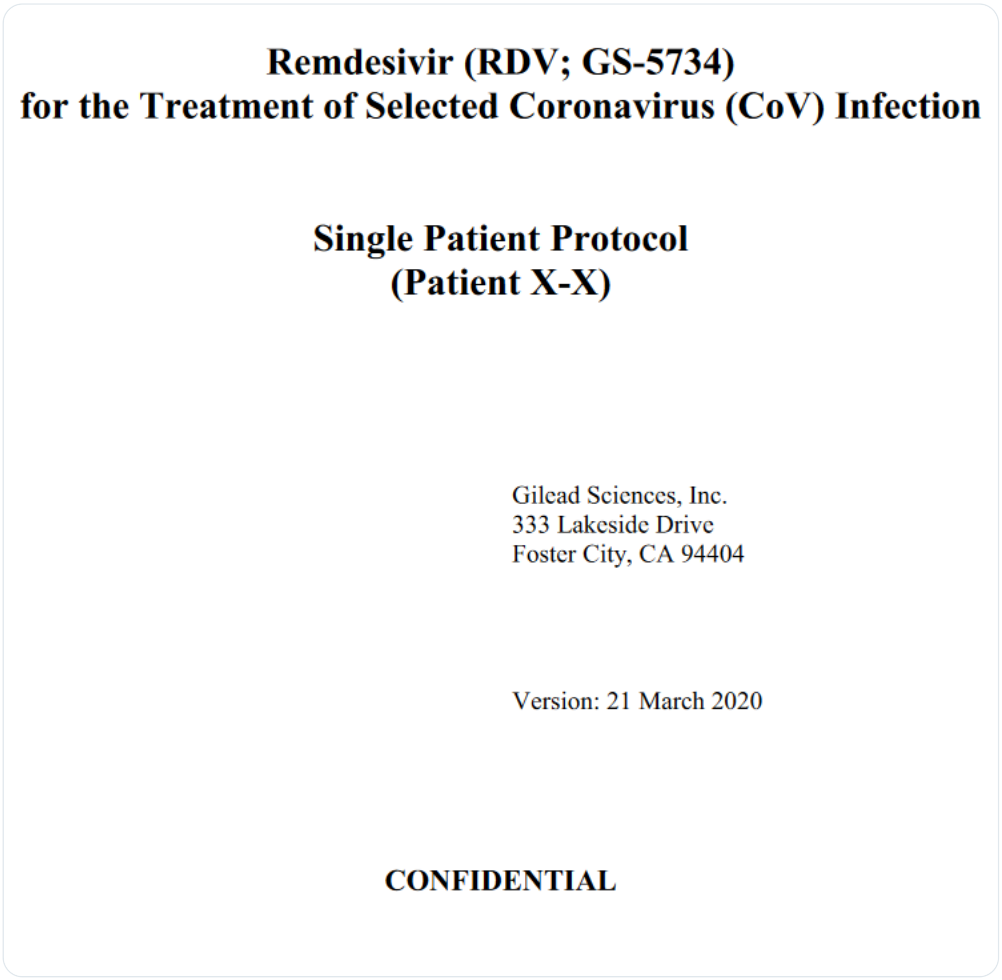
9🧵On page 73, virologist [not oncologist] Ralph Baric is awarded 11 grants totaling over $5.5m! 55% of which came by way of the NIAID & 36% came from Fauci's NIAID. The two most financed grants, each over $1million say so much about how they put the "plan" in "plandemic."



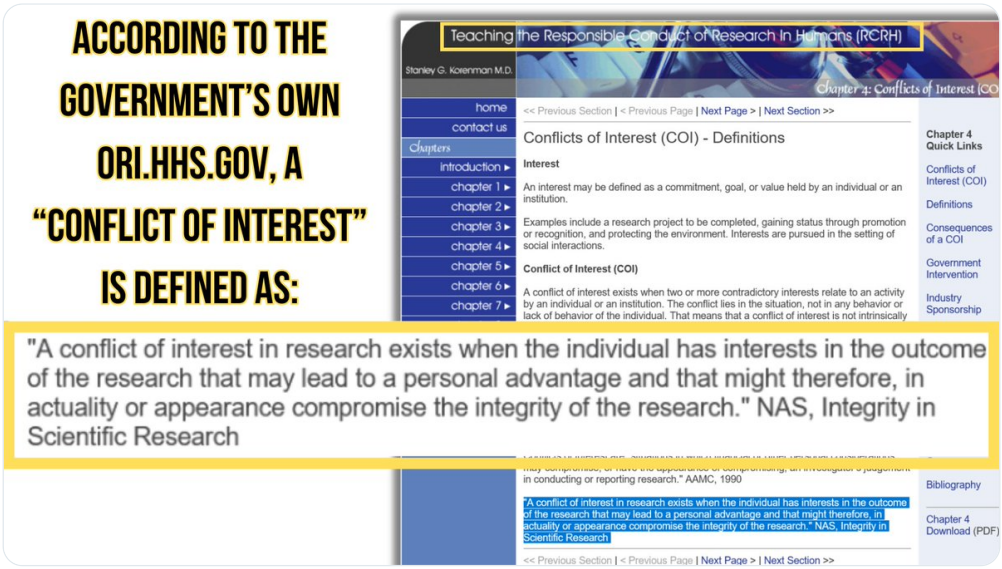


10🧵One grant for Baric was for looking into GS-5743 to "treat emerging coronaviruses" & the other million dollar grant was for "Respiratory Virus Vaccine & Adjuvants" Mind you, this is a 2019 report & GS-5743, btw, is the C19/Ebola poison, Remdesivir.





11🧵Lastly, I want to let the government & all implicated COVID criminals know that you guys are really good at playing the accidentally ignorant experts. You pretend your critics are conspiracy theorists but i know that YOU know the COIs/conspiracy plaguing you all. 👇U know!



12 🧾Receipts🔎

On behalf my friends, the vaccine injured: 🖕
You're gonna wish I took the jab, assholes. ✌️
I'm coming for the guilty. Bet on it. https://www.cancer.gov/research/key-initiatives/covid-19/serological-sciences-network/u54-centers-of-excellence
https://unclineberger.org/wp-content/uploads/sites/867/2019/11/UNC-Lineberger-UCRF-Report-FY19.pdf
https://www.nejm.org/doi/suppl/10.1056/NEJMoa2007016/suppl_file/nejmoa2007016_protocol.pdf
https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2930418-9

Sources:

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https://www.pnas.org/doi/full/10.1073/pnas.1707304114 https://nihrecord.nih.gov/sites/recordNIH/files/pdf/2017/NIH-Record-2017-06-30.pdf https://unclineberger.org/wp-content/uploads/sites/867/2019/11/UNC-Lineberger-UCRF-Report-FY19.pdf
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https://pubmed.ncbi.nlm.nih.gov/27578435/
https://www.scripps.edu/_files/pdfs/campuses/florida/annualreport2020.pdf
https://reporter.nih.gov/search/qkWL0AV0pUC-ztQD6umk-A/project-details/9328799
https://pubmed.ncbi.nlm.nih.gov/28807998/ https://grantome.com/grant/NIH/R01-AI127521-01A1
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My Sources?

https://usrtk.org/wp-content/uploads/2021/04/Saif-OSU-Batch-1.pdf
https://usrtk.org/wp-content/uploads/2022/12/UNC_Daszak-Media-Story.pdf
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https://journals.asm.org/doi/10.1128/jvi.03079-15
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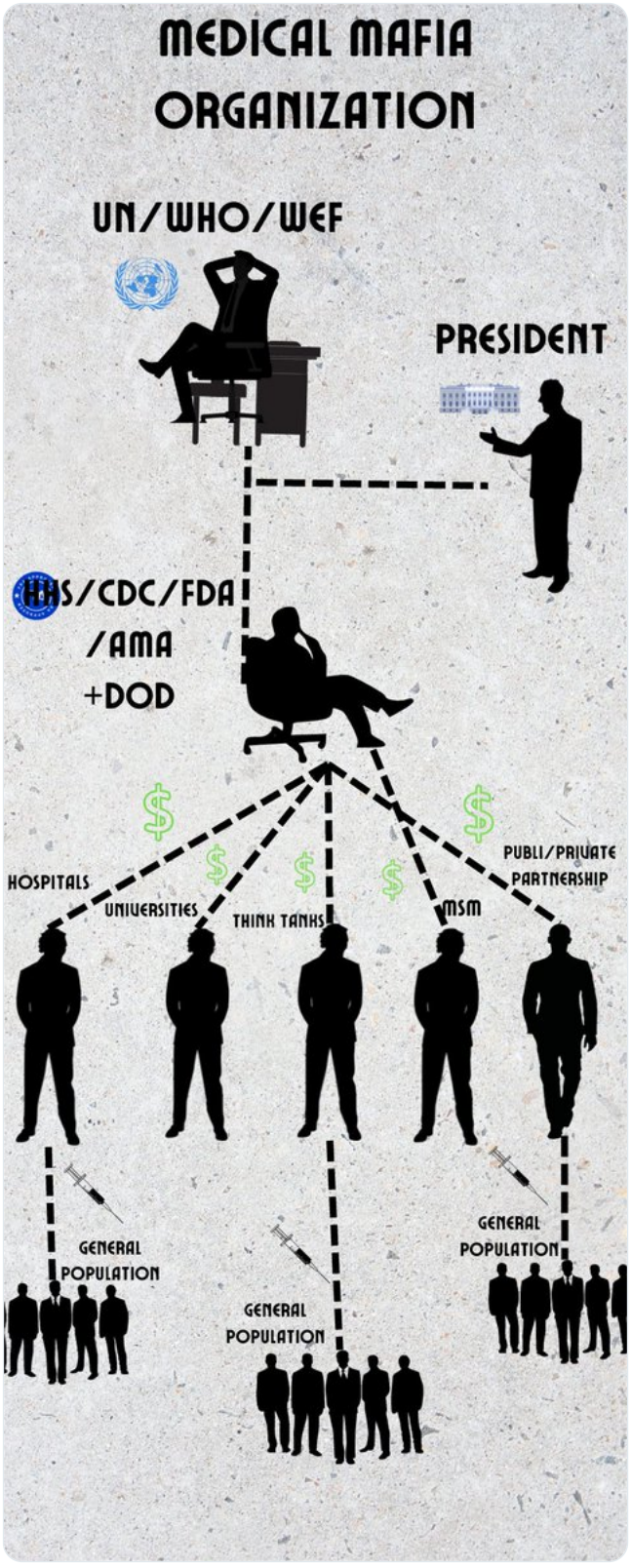
https://twitter.com/COVIDSelect/status/1730692429051826435



@threadreaderapp unroll

...

Destiny Rezendes @dezzie_rezzie

Dec 21, 2023 • 8 tweets • dezzie_rezzie/status/1737963752249520306

🚨1🧵The government MUST release the un-redacted complete Nov. 14, 2023 testimony of Peter Daszak. There must be a comparison between what he said in Nov. & what a set of freshly leaked DARPA proposals reveal.

2🧵The emails from Daszak [PD] to Baric [RB], Shi, & other EcoHealth [EH] staff on 2/7/2018 all review a draft proposal for DARPA in CoV research. RB may be able to alter viruses w/o being seen but he isn't nearly as skilled with editing grant proposals.

First (rough) draft of the DARPA abstract - Project DEFUSE

Peter Daszak <daszak@ecohealthalliance.org>

Wed 2/7/2018 8:51 PM

To: Ralph Baric (rbaric@email.unc.edu) <rbaric@email.unc.edu>; Wang Linfa <linfa.wang@duke-nus.edu.sg>; Zhengli Shi (zlshi@wh.iov.cn) <zlshi@wh.iov.cn>; William B. Karesh <karesh@ecohealthalliance.org>; Rocke, Tonie E <trocke@usgs.gov>
Cc: Luke Hamel <hamel@ecohealthalliance.org>; Jonathon Musser <musser@ecohealthalliance.org>; Anna Willoughby <willoughby@ecohealthalliance.org>; Kevin Olival, PhD <olival@ecohealthalliance.org>; Jon Epstein <epstein@ecohealthalliance.org>; Noam Ross <ross@ecohealthalliance.org>; Aleksei Chmura <chmura@ecohealthalliance.org>; Anna Willoughby <willoughby@ecohealthalliance.org>; Hongying Li <li@ecohealthalliance.org>

Dear All,

I've attached a first rough draft of the DARPA abstract. Apologies for the delay. Unfortunately, edits to my Science paper came through on Friday and took many hours to do, so this delayed me. I'm right now in Geneva in my hotel at 3 am finishing these off before flying back to NYC from a WHO meeting.

Some important points:

1) Zhengli, Linfa, Ralph – Billy and I spoke with Tonie Rocke on Friday. Tonie is at the National Wildlife Health Center, Madison USA, and has worked on wildlife vaccines: plague in prairie dogs, rabies in Jamaican fruit bats, white nose syndrome in US bats. We needed someone with expertise in delivery of molecules/vaccines to wildlife because DARPA specifically lay that out. As you'll see, Tonie is perfect for our project and will be able to do work at USGS NWHC and with Zhengli in China to help with TA2

?!

2) Zhengli and Linfa – After I spoke with you both, I had a great conversation with Ralph Baric. He proposed to work on recombinant chimeric spike proteins as a second line of attack. I think that is a perfect fit because 1) it's his expertise and he has published on it, 2) it will act as an alternative to the blue-sky and risky immune boosting work that Linfa/Peng have proposed. I hope you agree!

3) Ralph, Zhengli, Linfa, Tonie – as you can see, I have mangled the language/technical details for most of your sections. Pardon my lack of knowledge, and please draft a couple of paragraphs each to make your sections look correct. Thanks to Peng for giving me some text anyway – very useful, but please check what I've done with it.

4) All – please add some names and details on the team part so we get clarity in this on what staff you will need to do the work.

5) Please don't worry about keeping this to the 8 page limit. Just add text here and there, references, and edit to make what I've written correct, and more exciting. I will work on this on Saturday, Sunday and Monday to bring it down to 8 pages of very crisp, super-exciting text. I also want as many of your good ideas in here, so that I can use this draft to build on for the full proposal.

6) Finally – please edit rapidly using tracked changes in word. If you don't want to mess up endnote, please just insert references as comment boxes and we'll pull them off the web.

Aleksei and Anna: please read the draft and work on some draft image designs that sum up the project flow. I'll call you Thursday afternoon to discuss so you can finish them off.
Luke – please have a go at a first draft of the executive summary slide. I'll pick up from what you've done once you send it to me.

Thanks again to all of you for agreeing to collaborate on this proposal. From what I know of the competition, what DARPA wants, and what we're offering, I think we have an extremely strong team, so I'm looking forward to getting the full proposal together and winning this contract!

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
460 West 34th Street – 17th Floor
New York, NY 10001

Tel. +1 212-380-4473
www.ecohealthalliance.org

EcoHealth Alliance leads cutting-edge research into the critical connections between human and wildlife health and delicate ecosystems. With this science we develop solutions that prevent pandemics and promote conservation.

DARPA – PREEMPT – HR001118S0017

Abstract Submission Requirements:

**8 pages with 12 point font or higher (smaller font may be used for figures, tables and charts)

**Page limit includes all figures, tables, charts and the Executive Summary Slide

**Copies of all documents submitted must be clearly labeled with the following:

-DARPA BAA number

-Proposer Organization

-Proposal title/Proposal short title

-Submission letter is optional and does not count towards page limit

A. Cover Sheet (does not count towards page limit):

Include the administrative and technical points of contact (name, address, phone, fax, email, lead organization). Also include the BAA number, title of the proposed project, primary subcontractors, estimated cost, duration of project, and the label "ABSTRACT."

B. Executive Summary Slide:

Provide a one slide summary in PowerPoint that effectively and succinctly conveys the main objective, key innovations, expected impact, and other unique aspects of the proposed project. Use the slide template provided at http://www.fbo.gov.

****See slide template at bottom of document.**

PROJECT DEFUSE

C. Goals and Impact:

Clearly describe what is being proposed and what difference it will make (qualitatively and quantitatively), including brief answers to the following questions:

1. What is the proposed work attempting to accomplish or do?

We aim to **defuse the potential for emergence of novel bat-origin high-zoonotic risk SARS-related coronaviruses** in Southeast Asia. We envisage a scenario whereby the US warfighter is called on to intervene in a security hotspot in SE Asia for a period of 3-6 months. As planners begin choosing sites for the mission, they will use an app we will design to assess the background risk of a site harboring dangerous zoonotic viruses. If

spillover.

2. How is it done today? And what are the limitations?
Currently, there is no available technology to reduce the risk of exposure to novel coronaviruses from bats, other than avoid the regions where bats harbor these viruses. This includes large areas of southeast Asia where SARS-related CoVs are endemic in bats, which roost in caves during the day, but forage over wide areas at night, shedding virus in their feces and urine. The limitations of this lack of capacity are significant – we have shown evidence of recent spillover of SARS-related CoVs into people in southern China, and have identified viruses in this region that are capable of producing SARS-like illness in humanized mice, with no available vaccines or countermeasures. These viruses are a clear-and-present danger to our military personnel, and to global health security.

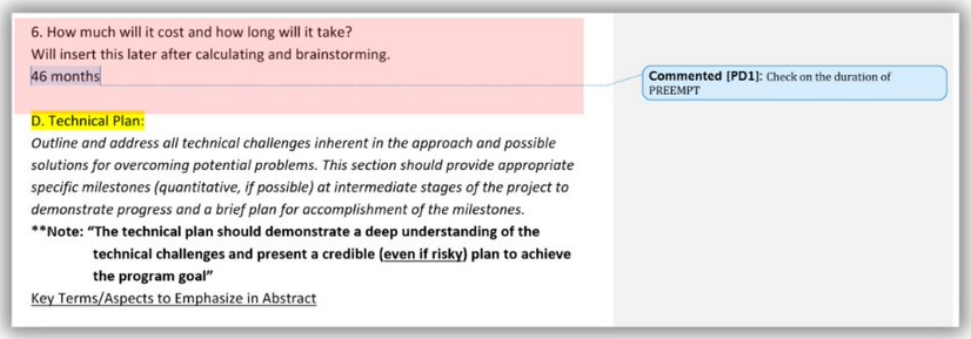
3. What is innovative in your approach and how does it compare to current practice and state-of-the-art (SOA)?
****Note: DARPA wants to know, "how the proposed project is revolutionary and how it significantly rises above the current state of the art**
Our group has shown that bats harbor the highest proportion of potential zoonoses of any mammal group, and that they are able to live with high viral loads due to unique damping of their immune systems, likely as an evolutionary adaptation to flight. We will use this to design strategies to upregulate their immune response in their cave roosts, down-regulate viral replication, and reduce the risk of viral shedding and spillover (immune boosting strategy). At the same time, we will inoculate bats with novel chimeric polyvalent recombinant spike proteins to enhance their immune response against replication of specific, high-risk viruses (immune priming strategy). We will use our innovative modeling to design apps that identify the likelihood of any region harboring high-risk bat viruses. We will design novel, automated approaches to deliver both types of inoculum remotely into caves to reduce exposure risk during decontamination.

4. What are the key technical challenges in your approach and how do you plan to overcome these?
Decide which of following parts to talk about:

3🧵They are clear with their intentions stating, "we will inoculate bats with novel chimeric polyvalent
recombinant spike proteins to enhance their immune response." they even list "Gain of Function"

Modeling bat suitability
Inventory of caves
Sampling/testing
Reverse engineering, binding assays, mouse expts
Modeling viral risk of evolution and spillover
Modeling inoculation/defusing strategy
Immune modulation
Immune Booster recombinant production
Gain-of-function issue.
Inoculum delivery
Mesocosm expts
Cave expts

5. Who will care and what will the impact be if you are successful?
This will have direct relevance to the warfighter. The potential for deployment to the region in which bat hosts of SARS-related CoVs exist is high – countries include security hotspots (Myanmar, Bangladesh, Pakistan, Lao, Korea). The ability to decontaminate and defuse these viruses will be useful in preventing potentially devastating illness. Furthermore, these technologies, if successful, can be adapted to hosts of other bat-origin CoVs (MERS, SADS), and potentially other zoonotic bat-origin viruses (Hendra, Nipah, EBOV). Finally, our approach is directly applicable to public health measures in the region to reduce the risk of spillover into the general population, as well as for food security by reducing the risk of viruses like SADS-CoV spilling over from bats into intensive pig farms, and devastating and industry, leading to potential civil unrest.


6. How much will it cost and how long will it take?
Will insert this later after calculating and brainstorming.
46 months

Commented [PD1]: Check on the duration of PREEMPT

D. Technical Plan:
Outline and address all technical challenges inherent in the approach and possible solutions for overcoming potential problems. This section should provide appropriate specific milestones (quantitative, if possible) at intermediate stages of the project to demonstrate progress and a brief plan for accomplishment of the milestones.
****Note: "The technical plan should demonstrate a deep understanding of the technical challenges and present a credible (even if risky) plan to achieve the program goal"**
Key Terms/Aspects to Emphasize in Abstract

by DARPA, including genome editing (CRISPR or RNAi), vaccination or DIP bats, in terms of its deployability and scalability. Finally, we will inoculate bats with fragments of non-bat Coronavirus (DETAILS).

Prof. Ralph Baric (UNC) will lead the immune priming work, building on his track record in reverse-engineering and manipulating SARS-CoV, MERS-CoV and other virus spike proteins over the last two decades . He will develop recombinant chimeric spike-proteins (*8*) based on SARSr-CoVs we have already identified, and those we will discover and characterize during project DEFUSE. RALPH – clearly I didn't really understand the details of your approach. Can you add a couple of paragraphs here and some citations please!

While there are clear advantages to working with fixed populations of cave-dwelling bats, molecule or vaccine delivery is technically challenging. Dr. Tonie Rocke, who developed, trialed, field-tested and rolled out the prairie dog plague vaccine (*9*), and is currently working on vaccines to bat rabies (*10, 11*) and white-nose syndrome, will manage a series of experiments in the lab and field to perfect a delivery system for both arms of TA2.

We will conduct initial experiments on a lab colony of wild-caught *Rhinolophus sinicus* bats at Wuhan Institute of Zoology. We (Prof. Wang) have previous experience conducting infection experiments on this bat genus …(details and citation if possible). First, we will use our recently proven technology to design LIPS assays to the specific high zoonotic-risk SARSr-CoVs (*12*). We will conduct serological analysis on bats captured for infection experiments, to assess prior exposure to specific strains. These LIPS assays will be made available for use in people to assess exposure of the general population around bat caves in China, and for potential use by the warfighter to assess exposure to SARSr-CoVs during combat missions.

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4🧵The attempt to lie for $ is clear; "I do want to stress the US side of this proposal so that DARPA are comfortable w/ our team. Once we get the funds, we can then allocate who does what exact work, & I believe that a lot of these assays can be done in Wuhan." says Daszak

distribution of bat hosts, we have access to biological inventory data on all bat caves in Southern China, as well as information on species distributions across SE Asia from the literature and museum records. We will use radio- and satellite telemetry to identify the home range of each species of bat in the caves, to assess how widely the viral 'plume' could contaminate surrounding regions, and therefore how wide the risk zone is for the warfighter positioned close to bat caves.

We will build environmental niche models using the data above, and environmental and ecological correlates, and traits of cave species communities (eg. phylogenetic and functional diversity), to predict the species composition of bat caves across Southern China, South and SE Asia. We will validate these with data from the current project and data from PREDICT sampling in Thailand, Indonesia, Malaysia and other SE Asian countries. We will then use our unique database of bat host-viral relationships updated from our recent *Nature* paper (*1*) to assess the likelihood of low- or high-risk SARSr-CoVs being present in a cave at any site across the region. At the end of Yr 1, we will use these analyses to produce a prototype app for the warfighter that identifies the likelihood of bats harboring dangerous viral pathogens based on these analyses. **The 'high-risk bats near me' app** will be updated as new host-viral surveillance data comes on line from our project and others, to ground-truth and fine-tune its predictive capacity. Specifically, our telemetry data on bat movement will be used to assess how often bats from high-risk caves migrate to other colonies and potentially spread their high-risk strains.

The Wuhan Institute of Virology team will conduct viral testing on samples from all bat species in the caves as part of this inventory. Fecal, oral, blood and urogenital samples will be collected from bats using standard capture techniques as we have done for the last decade. In addition, tarps will be laid down in caves to assess the feasibility of surveys using pooled fresh fecal and urine samples. Assays will be designed to correlate viral load in an individual with viral shedding in a fecal sample. Once this is complete, surveys will continue largely on fecal samples so as not to disturb bat colonies and undermine longitudinal sampling capacity. Samples will be tested by PCR and spike proteins of all SARS-related CoVs sequenced. Analyses of phylogeny, recombination events, and further characterization of high-risk viruses (those with spike proteins close to SARS-CoV) will be carried out (REF). Isolation will be attempted on a subset of samples with novel SARSr-CoVs. Prof. Ralph Baric, UNC, will reverse engineer spike proteins in his lab to conduct binding assays to human ACE2 (the SARS-CoV receptor). Proteins that bind will then be inserted into SARS-CoV backbones, and inoculated into humanized mice to assess their capacity to cause SARS-like disease, and their ability to be blocked by monoclonal therapies, or vaccines against SARS-CoV (REF).

The modeling team will use these data to build models of 1) risk of viral

Commented [PD3]: Could add " We will continue monitoring the human population proximal to these caves to assess the rates of viral spillover, and ground-truth which specific CoVs are able to infect people

"*Once we get the funds* we can then allocate who doe what exact work and I believe that a lot of these assays can be done in Wuhan.."

Commented [PD4]: Ralph, Zhengli. If we win this contract, I do not propose that all of this work will necessarily be conducted by Ralph, but I do want to stress the US side of this proposal so that DARPA are comfortable with our team. Once we get the funds, we can then allocate who does what exact work, and I believe that a lot of these assays can be done in Wuhan as well...

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Team:
Lead Organization: EcoHealth Alliance, New York
PI: Peter Daszak Ph.D., President & Chief Scientist, EcoHealth Alliance, 3 months/year
Key Personnel:
Billy Karesh DVM, Executive VP for Policy & Health, 1 month/year
Kevin J. Olival Ph.D, VP for Scientific Research, 1 month/year
Jonathan H. Epstein DVM Ph.D., VP for Science & Outreach, 0.5 months/year
Carlos Zambrana-Torrelio Ph.D., Assoc. VP for Conservation & Health, 1 month/year
Noam Ross Ph.D., Senior Research Scientist, 2 months/year
Evan Eskew, Research Scientist, 2 months/year
Hongying Li, Program Coordinator, China Programs, 3 months/year
TBD Postdoctoral Researcher modeling and analysis, 12 months/year
TBD Research Assistant, 12 months/year
TBD Program Assistant, 12 months/year
Guangjian Zhu Ph.D., Consultant Field Lead, China Programs, 6 months/year
Yunzhi Zhang Ph.D., Consultant, Yunnan CDC, China, 2 months/year

Subcontract #1: University of North Carolina Medical School
Organizational Lead: Prof. Ralph Baric Ph.D., 2 months/year
XXX
TBD Research Assistant, 12 months/year

Subcontract #2: USGS National Wildlife Health Center
Organizational Lead: Tonie Rocke Ph.D., 2 months/year, no salary requested
TBD Research Technician, 9 months/year

Subcontract #3: Duke NUS, Singapore
Organizational Lead: Prof. Linfa Wang Ph.D., 2 months/year
XXX
TBD Research Assistant, 12 months/year
XXX

Subcontract #4: Wuhan Institute of Virology, China
Organizational Lead: Prof Zhengli Shi Ph.D., 2 months/year
Peng Zhou Ph.D., 2 months/year
TBD Research Assistant, 12 months/year

5🧵Methods planned in the draft say "aerosolization" & "transdermally applied Nanoparticle." Baric & Daszak try to downplay Shi/WIVs role in the work despite noting that DARPA would dislike it, & the BSL2 labs in China were handling SARS- a BSL3 selected agent.

ARC - aerosols

William B. Karesh (b) (6) @gmail.com>
Fri 2/2/2018 12:34 PM
To: Rocke, Tonie E <trocke@usgs.gov>; Peter Daszak <daszak@ecohealthalliance.org>
Cc: Luke Hamel <hamel@ecohealthalliance.org>

1 attachments (438 KB)
PARC.pdf;

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www.parc.com

Project Overview

- PARC developed a unique spray technology for large area and high throughput aerosol delivery of highly viscous and concentrated fluids. These fluids can include a range of solutions, e.g., bioactive formulations. This technology has a potential application in large area inoculation of animals/humans with bioengineered formulations for pre-emptive reduction of disease transfer.
- PARC has expertise in fluid/aerosol delivery, leveraging the unique spray method that can aerosolize fluids independent of viscosity or bioactive concentration. This technique enables partners in the biological space to deliver bioactive formulations to animal models with improved chance of efficacy/bioavailability. Potential technical challenges to overcome will be systems integration with rapid development/preparation of pre-emptive agents (potentially with on-demand concentration and composition) and in testing the biological response with animal models.
- PARC can have significant involvement in Technical Area 2 of a PRE-EMPT project: development of a scalable aerosol delivery method for wide-scale inoculation of animal models.

Teaming Overview and Objectives

- PARC has worked with both commercial and university partners for applications of this technology.
- PARC has expertise in fluid delivery, droplet generation, and device and systems integration drawing on our long history with developing printing systems (ink-on-paper). PARC will leverage both previous and on-going work and our related IP portfolio on fluid delivery using platform technologies (spray, transdermal delivery) to meet the PRE-EMPT program objectives.
- PARC has the institutional assets to develop and fabricate new systems for spraying, as well as the background to help improve spray formulation for uptake in mucosal and other targeted membranes.
- PARC is well-positioned to advance its unique spray technology for the PRE-EMPT program, given its demonstrated scalability and wide applicability across different fluids (ranging from low to very high viscosity and independent of bioactive concentration/loading). PARC is looking for collaborators who will investigate disease transmission across animal species and develop the necessary pre-emptive biologicals to prevent such transmission. These engineered biologicals can then be delivered to animal models using the spray technology with maximum chance for efficacy and bioavailability.

Contact Information

Dr. Jerome Unidad; email: Jerome.Unidad@parc.com; telephone: 650-812-4209

by DARPA, including genome editing (CRISPR or RNAi), vaccination or DIP bats, in terms of its deployability and scalability. Finally, we will inoculate bats with fragments of non-bat Coronavirus (DETAILS).

Prof. Ralph Baric (UNC) will lead the immune priming work, building on his track record in reverse-engineering and manipulating SARS-CoV, MERS-CoV and other virus spike proteins over the last two decades . He will develop recombinant chimeric spike-proteins (*8*) based on SARSr-CoVs we have already identified, and those we will discover and characterize during project DEFUSE. RALPH – clearly I didn't really understand the details of your approach. Can you add a couple of paragraphs here and some citations please!

While there are clear advantages to working with fixed populations of cave-dwelling bats, molecule or vaccine delivery is technically challenging. Dr. Tonie Rocke, who developed, trialed, field-tested and rolled out the prairie dog plague vaccine (*9*), and is currently working on vaccines to bat rabies (*10, 11*) and white-nose syndrome, will manage a series of experiments in the lab and field to perfect a delivery system for both arms of TA2.

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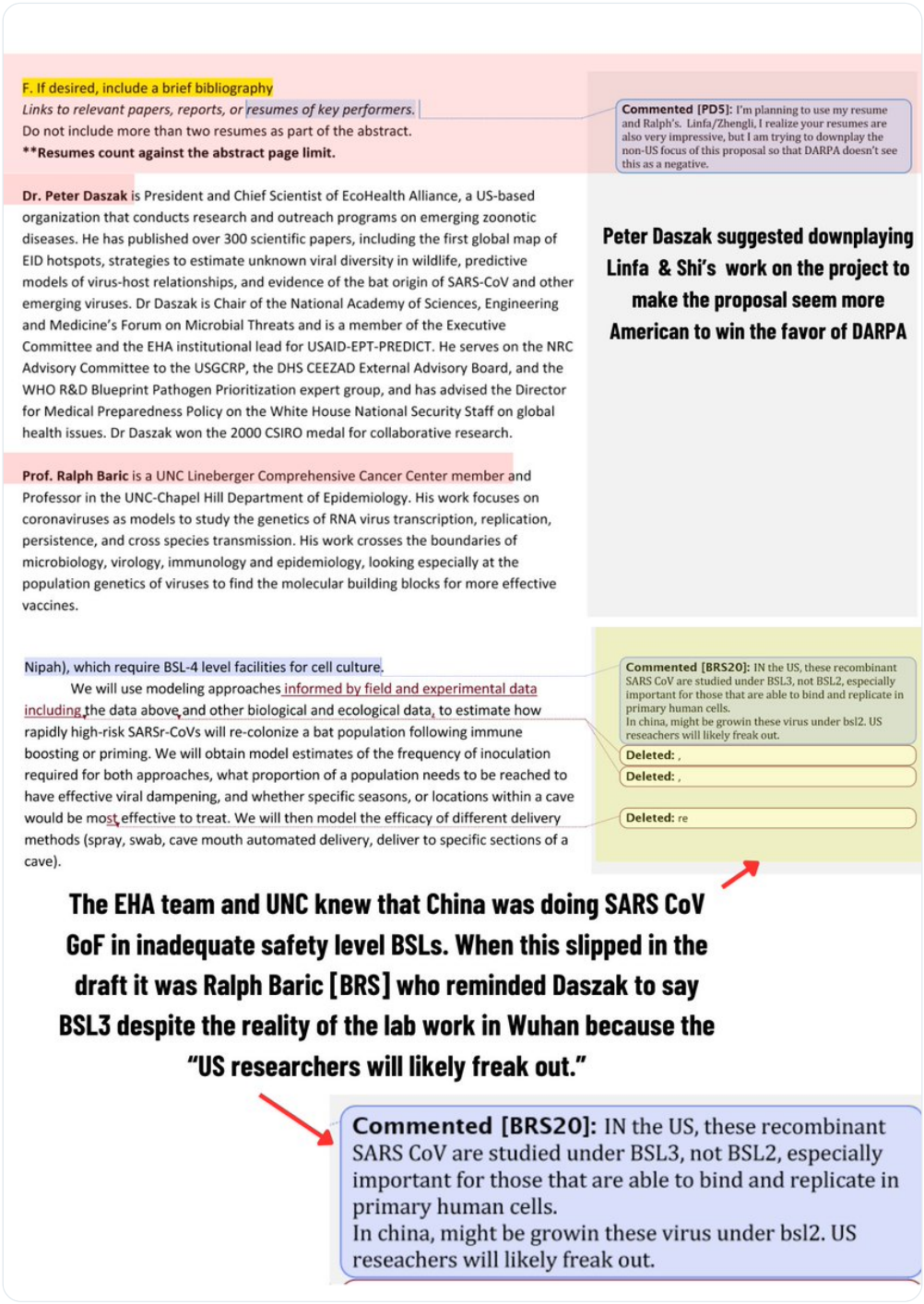
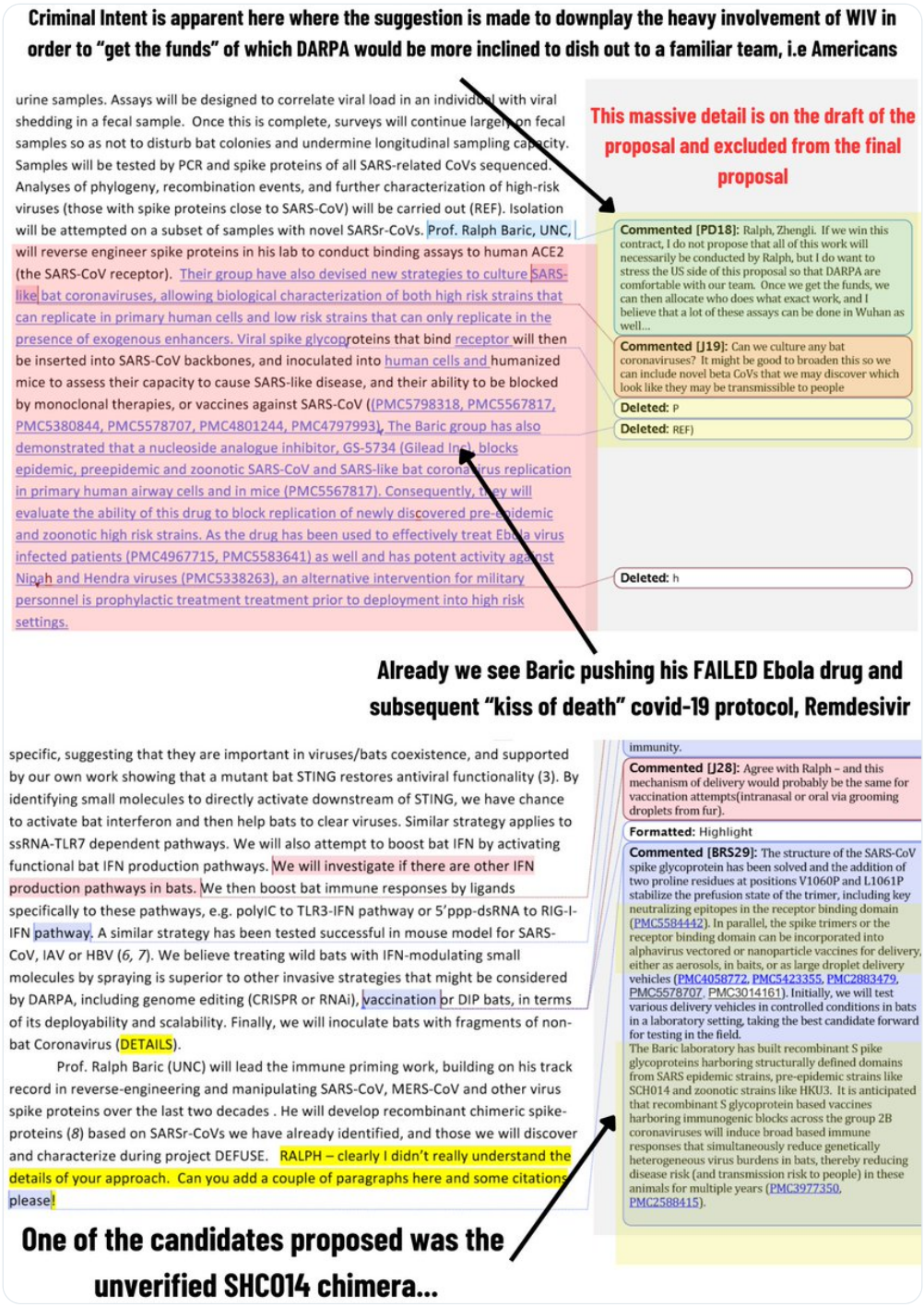


6🧵The plan was to use aerosolized agents to inoculate the bat caves in China, chimerically alter the viruses, enhance them & create biologics. Oh, and also for RBS to try to re-purpose his FAILED Ebola poison, Remdesivir [GS-5734] to use it for CoV [which he later did for Covid-19]🤫 Also, the undocumented chimera SHC014 cited for use. Daszak's 5+wk old testimony has yet to be released-which begs the question; What else are they hiding? Until our leaders take the initiative, we won't know. People, no, BILLIONS of people have lost; jobs, education, loved ones, livelihoods, freedoms and normalcy for 3 years. There was crimes committed in this pandemic. WE did the hard time..now it's time that the criminals do theirs.



Source : https://usrtk.org/wp-content/uploads/2023/12/2021-006245-Combined-Records_Redacted-1-235.pdf

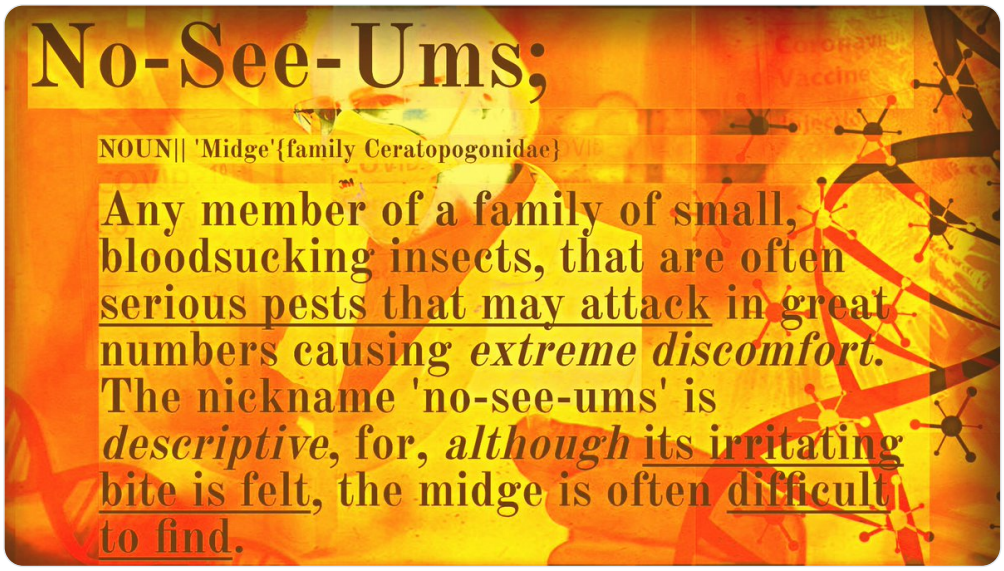
@threadreaderapp unroll

...

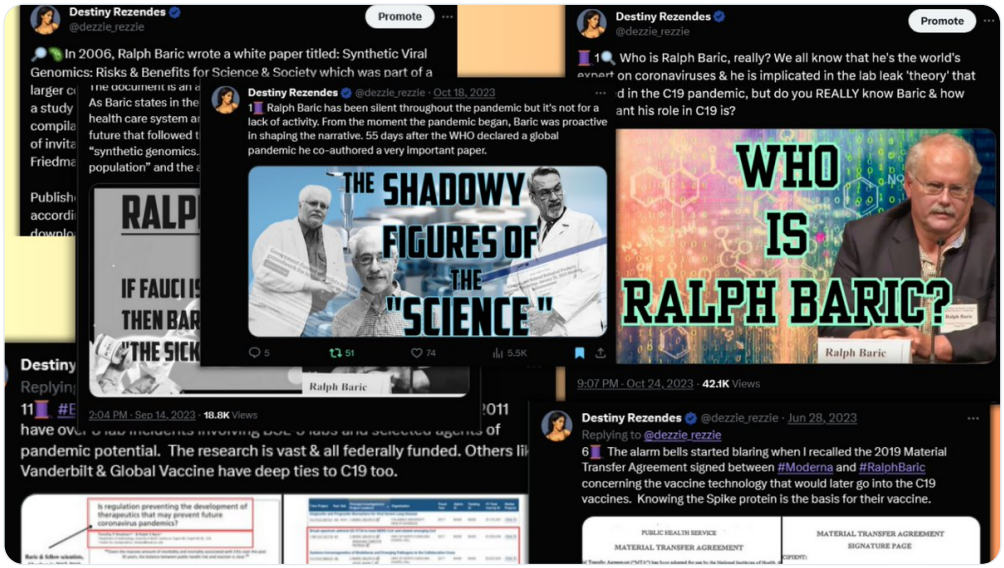
Destiny Rezendes @dezzie_rezzie

Feb 6, 2024 • 10 tweets • dezzie_rezzie/status/1754684068334092750

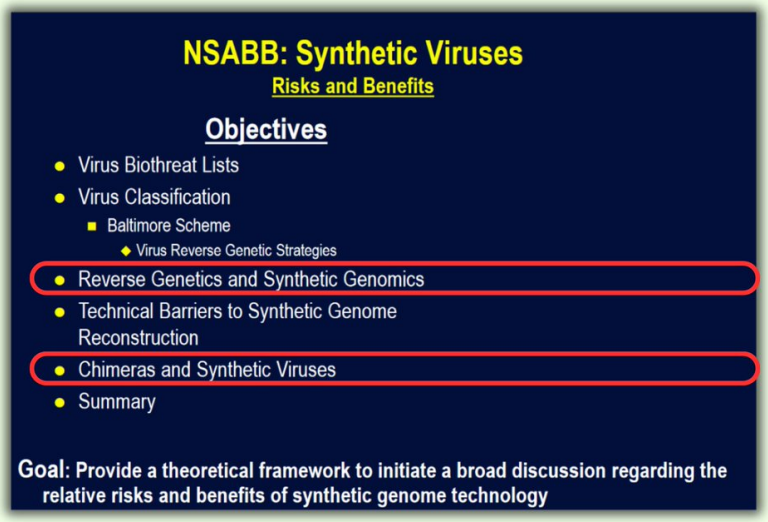
🧵1🧵Ralph Baric invented No-See-Um sites, a way to alter viruses w/o leaving a trace. The name comes from bugs local to Baric in NC. Oddly the definition of No-See-Ums describes not just the bugs, but also Baric himself. So, why did NIH allow this infestation to go unchecked?!



2🧵I've covered the Corona-Creep at length. For today's thread familiarizing yourself [if you haven't] with these threads- namely this thread about Baric's publication on Synthetic Biology 2006:



3🧵The same yr as Baric's terrifying Synthetic Genomic paper, Baric gave a presentation to the National Science Advisory Board for Biosecurity [NSABB] on Synthetic Viruses. The NSABB is the federal advisory committee that addresses threats to biosecurity and Gain of Function.



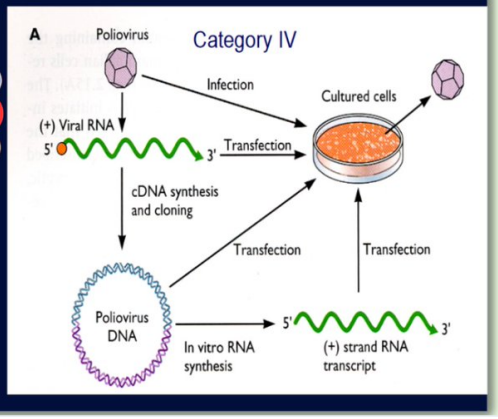
4🧵 Per Baric's NSABB presentation, Biothreat Viruses that can be created in a lab or "reverse engineered" have understood mechanisms; for instance "ALL viruses MUST transcribe genome into mRNA *for making* Viral Proteins." He lists, SARS-CoVs as easy to alter, & that the sequences to do so are "readily available."

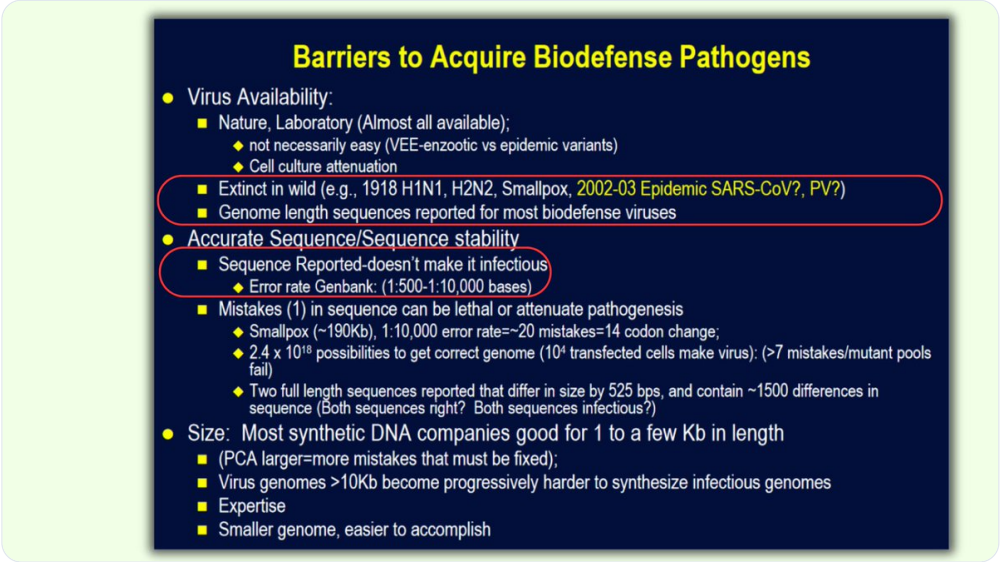
Biothreat Viruses
HHS/CDC, USDA, Dept Commerce, NIH Category A-C
(Lists of Biothreat Viruses)

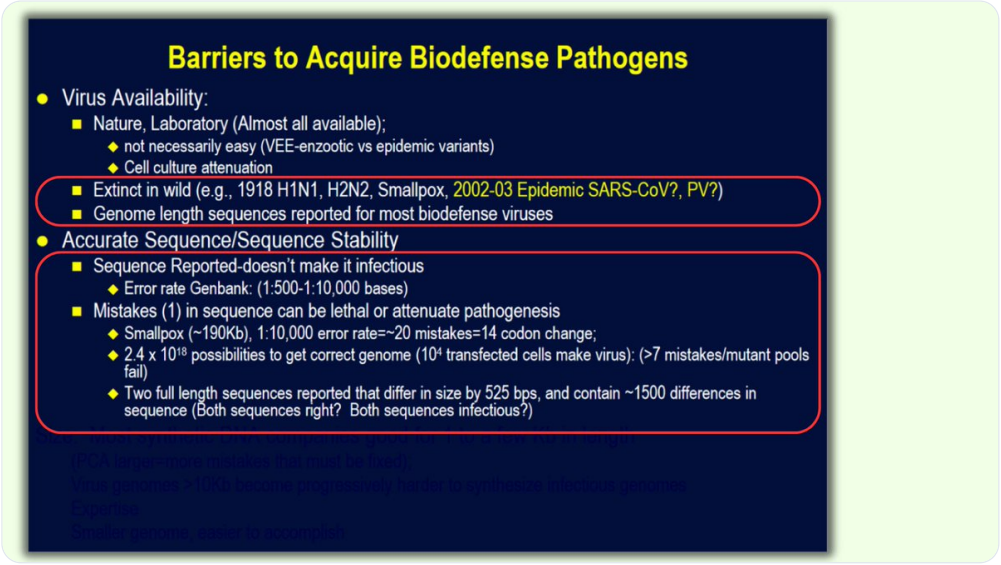
- Very Heterogeneous group of viruses
  - HHS/CDC, USDA, Dept Commerce (Lists of Biothreat Viruses)
- Different genome organizations + replication strategies
  - different approaches are needed to develop infectious genomes
  - Genomes
    - dsDNA, ssRNA (+) polarity, ssRNA (-) polarity and dsRNA
- Simple classification scheme to understand virus reverse genetic strategies
  - All viruses must transcribe genome into mRNA ⟶ viral proteins.

Virus Reverse Genetics
Category IV

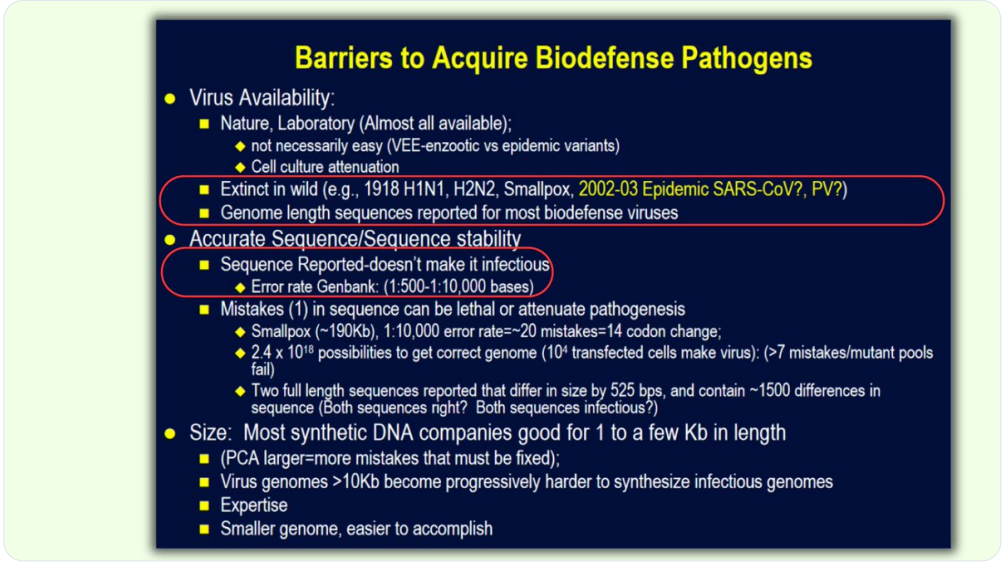
- Positive Strand RNA Viruses
  - Picornaviruses
  - Enteroviruses (e.g., PV, FMDV, HAV)
  - Coronaviruses (e.g., SARS-CoV)
  - Alphaviruses (e.g., VEE, WEE, EEE)
  - Flaviviruses (e.g., Yellow fever, dengue, etc.)
  - Noroviruses (not yet)
- Manipulate DNA and recover altered viruses
- Sequences readily available

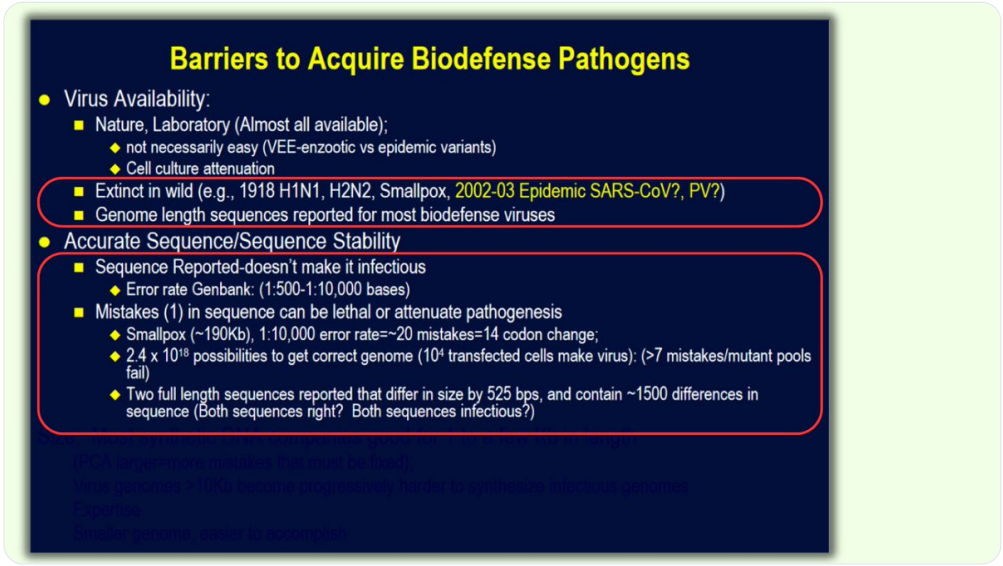






5 For barriers to biodefense Baric admits that Sequence Stability is a concern, stating that "Sequences Reported doesn't make it infectious" & that even NIH's Genbank has an alarming Error Rate of anywhere between 1:500- 1:10,000 bases! These "mistakes" can make a pathogen more lethal or attenuate parthenogenesis. 👀

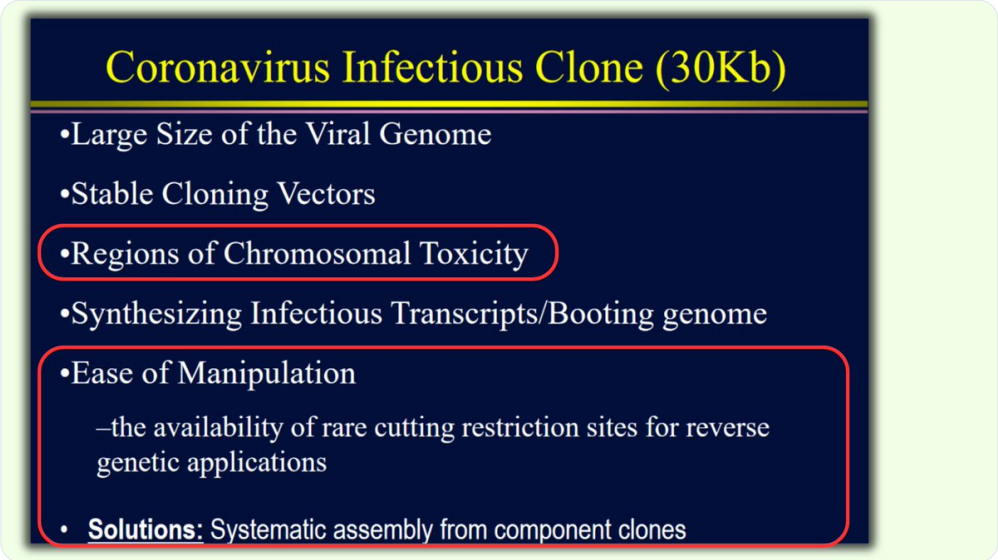




6🧵 When talking specifically about Coronavirus Infectious Clones are the easiest to manipulate but notes they have regions of "Chromosomal Toxicity."

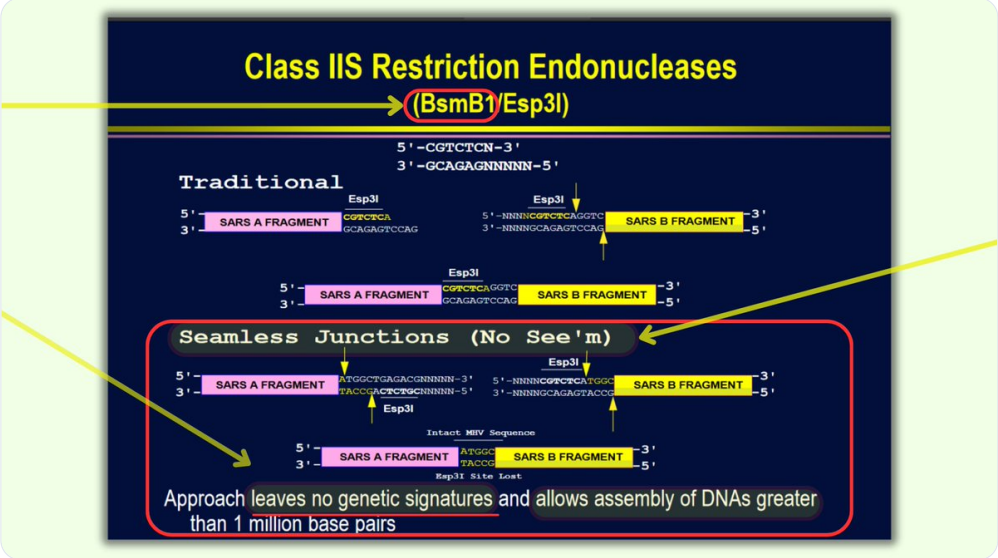
Well, what does that even mean? ⁉️

According to the NIH, Chromosomal toxicity refers to the harmful effects on the chromosomes within a cell, which can lead to DNA damage, mutations, and potentially CANCER!! ☠️



7🧵 On one slide, Baric gives the NSABB an example for how easily Coronavirus no-see-um-manipulation is done. Take note of which restriction site Endonuclease Enzymes Baric suggests: Esp31 & BsmB1.

The SAME one cited in the DARPA DEFUSE draft by EcoHealth Alliance + Ralph Baric from 2018 where they suggested its use to create pathogenic SARS-CoV chimera's. This is merely a coincidence, & even if it wasn't how could you prove it when Baric himself brags by adding to the BsmB1 slide that this "Approach leaves NO GENETIC SIGNATURES.."



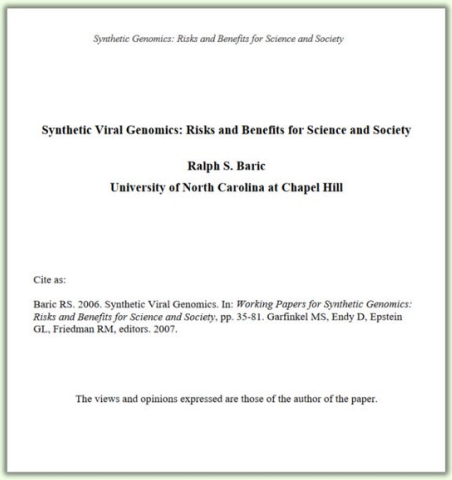
8🧵 A quick look back at that Synthetic Biology paper Baric authored in 2006 focused on Synthetic Viruses & Biological Warfare. On one page, Baric describes how a Bioterrorist would deploy these pathogens. The nonchalant way he describes these scenarios is cause for alarm all on it's own, but the actual text is a biological nightmare.

🚨👇✍️

Baric writes;

"A clever bioterrorist might start with a relatively benign, easily obtainable virus (BSL2) & obtain an existing molecular clone by simply requesting it from the scientists who work with these agents. Then, using the expanding database of genomic sequences & identified virulence genes, the benign viral genome

could be modified into more lethal combinations for nefarious use."



Synthetic Genomics: Risks and Benefits for Science and Society

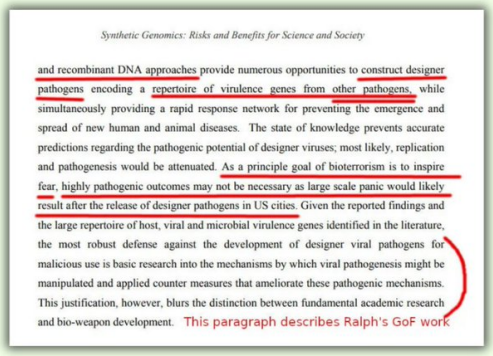
Synthetic Viral Genomics: Risks and Benefits for Science and Society

Ralph S. Baric
University of North Carolina at Chapel Hill

Cite as:

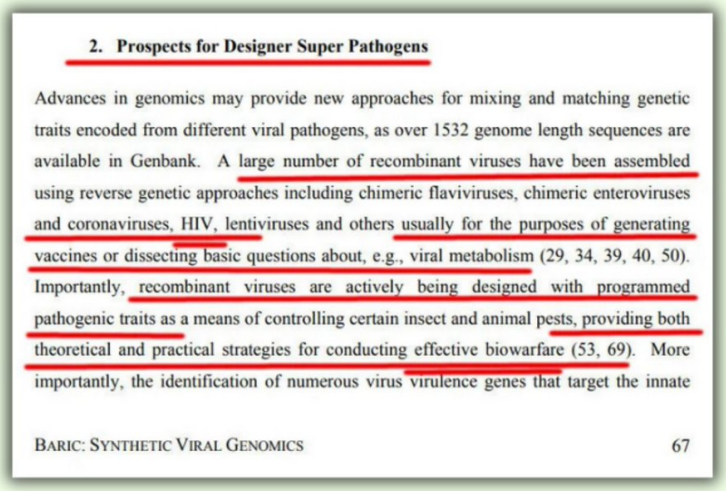
Baric RS. 2006. Synthetic Viral Genomics. In: *Working Papers for Synthetic Genomics: Risks and Benefits for Science and Society*, pp. 35-81. Garfinkel MS, Endy D, Epstein GL, Friedman RM, editors. 2007.

The views and opinions expressed are those of the author of the paper.



Synthetic Genomics: Risks and Benefits for Science and Society

and recombinant DNA approaches provide numerous opportunities to construct designer pathogens encoding a repertoire of virulence genes from other pathogens, while simultaneously providing a rapid response network for preventing the emergence and spread of new human and animal diseases. The state of knowledge prevents accurate predictions regarding the pathogenic potential of designer viruses; most likely, replication and pathogenesis would be attenuated. As a principle goal of bioterrorism is to inspire fear, highly pathogenic outcomes may not be necessary as large scale panic would likely result after the release of designer pathogens in US cities. Given the reported findings and the large repertoire of host, viral and microbial virulence genes identified in the literature, the most robust defense against the development of designer viral pathogens for malicious use is basic research into the mechanisms by which viral pathogenesis might be manipulated and applied counter measures that ameliorate these pathogenic mechanisms. This justification, however, blurs the distinction between fundamental academic research and bio-weapon development. This paragraph describes Ralph's GoF work



2. Prospects for Designer Super Pathogens

Advances in genomics may provide new approaches for mixing and matching genetic traits encoded from different viral pathogens, as over 1532 genome length sequences are available in Genbank. A large number of recombinant viruses have been assembled using reverse genetic approaches including chimeric flaviviruses, chimeric enteroviruses and coronaviruses, HIV, lentiviruses and others usually for the purposes of generating vaccines or dissecting basic questions about, e.g., viral metabolism (29, 34, 39, 40, 50). Importantly, recombinant viruses are actively being designed with programmed pathogenic traits as a means of controlling certain insect and animal pests, providing both theoretical and practical strategies for conducting effective biowarfare (53, 69). More importantly, the identification of numerous virus virulence genes that target the innate

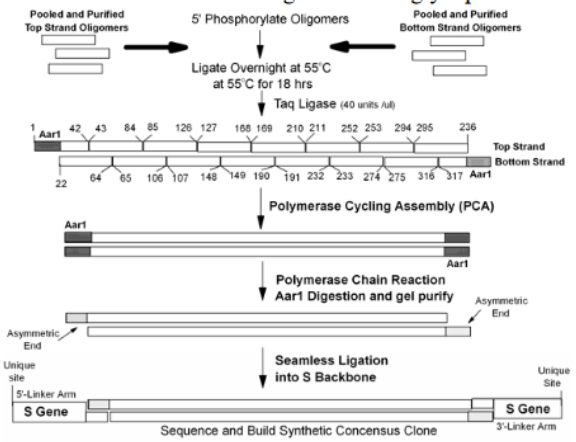
Synthetic Genomics: Risks and Benefits for Science and Society

engineering tools have been developed for only a few BW agents, making them relatively poor substrates for biodesign. A clever bioterrorist might start with a relatively benign, easily obtainable virus (BSL2) and obtain an existing molecular clone by simply requesting it from the scientists who work with these agents. Then, using the expanding database of genomic sequences and identified virulence genes, the benign viral genome could be modified into more lethal combinations for nefarious use.

Consequently, knowledgeable experts can theoretically reconstruct full length synthetic genomes for any of the high priority virus pathogens, although technical concerns may limit the robustness of these approaches. It is conceivable that a bioterrorist could order

Figure 9. PCA Technique. Synthetic Reconstruction of Exotic SARS-CoV Spike Glycoproteins.

Synthetic S glycoproteins are synthesized and inserted into the SARS-CoV molecular clone; allowing for recovery of recombinant viruses encoding zoonotic S glycoproteins.



9 Baric also writes what he thinks a BioTerror attack using a lab created virus would look like. You tell me if his description sounds familiar... "the release & subsequent discovery of a synthetically derived virus bioweapon will certainly garner tremendous media coverage, inspire fear & terrorize human populations."

Will synthetic or recombinant bioweapons be developed for BW use? If the main purpose is to kill and inspire fear in human populations, natural source pathogens likely provide a more reliable source of starting material. Stealing the BW agent from a laboratory or obtaining the pathogen from natural outbreak conditions is still easier than the synthetic reconstruction of a pathogenic virus. These conditions, however, change as 1st and 2nd generation candidate vaccines and drugs are developed against this select list of pathogens, limiting future attempts to newly emerged viruses. If notoriety, fear and directing foreign government policies are principle objectives, then the release and subsequent discovery of a synthetically derived virus bioweapon will certainly garner tremendous media coverage, inspire fear and terrorize human populations and direct severe pressure on government officials to respond in predicted ways.

10 Lastly, remember what Baric said about the benefits of his synthetic No-See-Um method compared to prior/classic techniques;

"Recombinant viruses generated from classic recombinant DNA techniques will carry the signature of the parental virus used in the process as well as novel restriction sites that were engineered into the genome during the cloning process.

In contrast, synthetic viral genomes can be designed to be identical with exact virus strains circulating in any given location from any year. This powerful technique provides the bioterrorist with a “scapegoat” option; leaving a sequence signature that misdirects efforts at tracking the true originators of the crime."

The only question you should have is since this is true and well documented then WHY has congress NOT called Ralph Baric in to publicly testify or at least be thoroughly investigated.
It's a tough and ugly question that likely won't be resolved and that's because the answer may very well be much, much, MUCH worse. 🔍

during the cloning process. In contrast, synthetic viral genomes can be designed to be

identical with exact virus strains circulating in any given location from any year. This powerful technique provides the bioterrorist with a "scapegoat" option; leaving a sequence signature that misdirects efforts at tracking the true originators of the crime. Even better, the approach could be used to build mistrust and/or precipitate open warfare between nations. A simple example might involve the use of the picornavirus foot and mouth disease virus, which is not present on the North American continent, yet is

1st and 2nd generation candidate vaccines and drugs are developed against this select list of pathogens, limiting future attempts to newly emerged viruses. If notoriety, fear and directing foreign government policies are principle objectives, then the release and subsequent discovery of a synthetically derived virus bioweapon will certainly garner tremendous media coverage, inspire fear and terrorize human populations and direct severe pressure on government officials to respond in predicted ways.

2. Prospects for Designer Super Pathogens

Advances in genomics may provide new approaches for mixing and matching genetic traits encoded from different viral pathogens, as over 1532 genome length sequences are available in Genbank. A large number of recombinant viruses have been assembled using reverse genetic approaches including chimeric flaviviruses, chimeric enteroviruses and coronaviruses, HIV, lentiviruses and others usually for the purposes of generating vaccines or dissecting basic questions about, e.g., viral metabolism (29, 34, 39, 40, 50). Importantly, recombinant viruses are actively being designed with programmed pathogenic traits as a means of controlling certain insect and animal pests, providing both theoretical and practical strategies for conducting effective biowarfare (53, 69). More importantly, the identification of numerous virus virulence genes that target the innate


GS-5734
R.Baric
RESOURCES:
https://osp.od.nih.gov/wp-content/uploads/Baric-Synthetic_Viruses_Risks_and_Benefits.pdf
https://dspace.mit.edu/bitstream/handle/1721.1/39652/Baric%20Synthetic%20Viral%20Genomics.pdf
https://comedonchisciotte.org/la-descrizione-di-ralph-baric-dellarma-biologica-perfetta-sembra-terribilmente-simile-al-sars-cov-2/
MRNA-1273

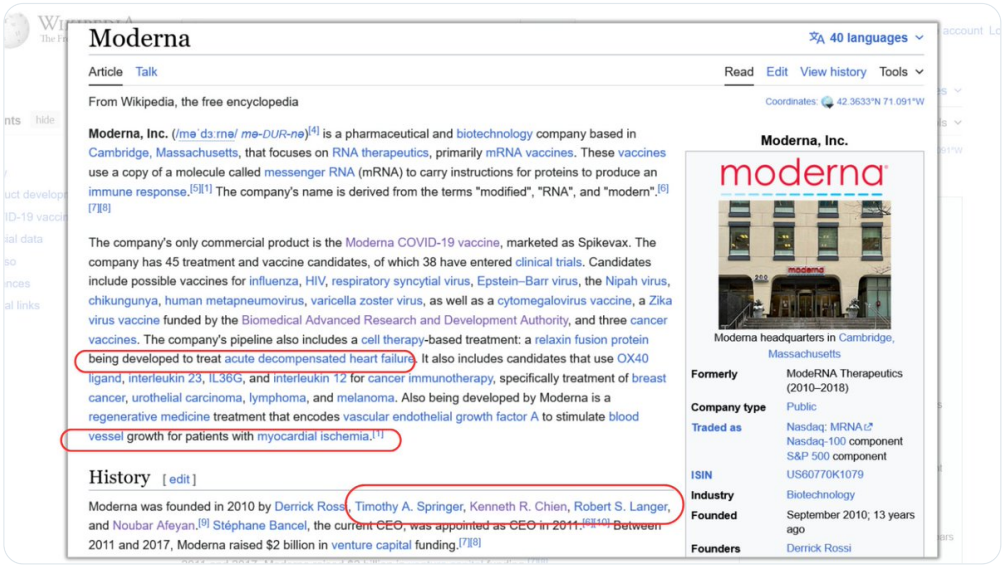
• • •

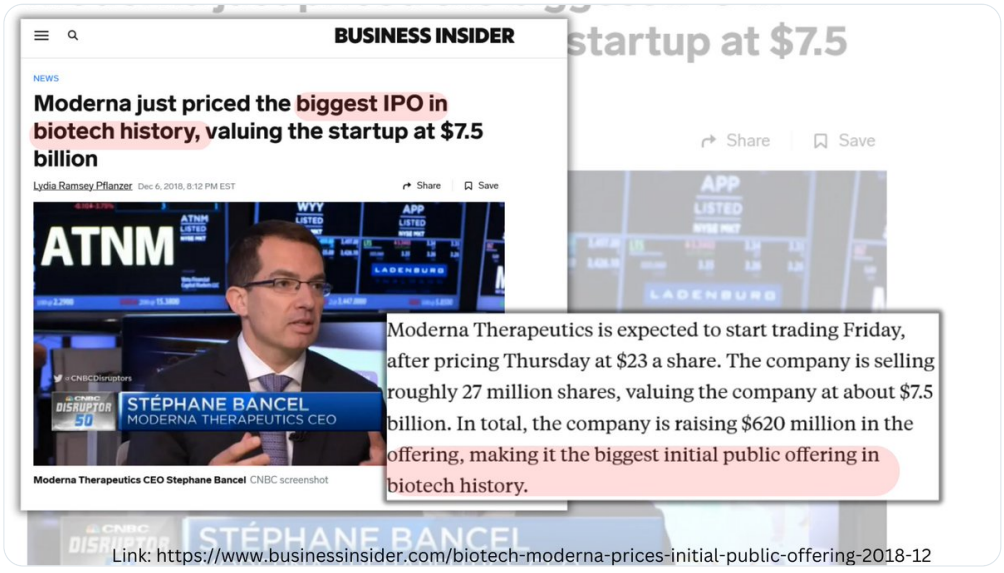
Destiny Rezendes @dezzie_rezzie

Feb 9, 2024 • 12 tweets • dezzie_rezzie/status/1756053850694287636

1🧵There is nothing that anyone can tell me to convince me that Ralph Baric of UNC Chapel Hill is an innocent character in the C19 Pandemic & neither is DARPA. By the end of this thread I'm sure you'll agree with me. [Buckle up, folks]

2🧵Let's start with Moderna, the company that Baric signed a Material Transfer Agreement [MTA] w/ in 2015, 2017, & 2019. Moderna had simultaneously signed a MTA with NIH's Vaccine Research Center [VRC] for mRNA CoV vaccine platform.





Link: https://www.businessinsider.com/biotech-moderna-prices-initial-public-offering-2018-12

3🧵 Now, Moderna was a new startup that prior to C19 hadn't brought a vaccine to market, they did however in 2013 joined DARPA for a $25M dollar project called ADEPT-PROTECT, whose stated goal is: Rapid development & deployment of medical countermeasures (MCMs) based on the encoding of antibodies in RNA and DNA. That's 25million of tax payer dollars to a company that had yet been successful by any meaningful measure. Moderna at the time was only 3 years old.

Product development [edit]

In 2013, the company formed a partnership with AstraZeneca to develop treatments for cardiovascular, metabolic, and renal diseases, as well as cancer. Moderna also was awarded a $25,000,000 grant by DARPA through a program Autonomous Diagnostics to Enable Prevention and Therapeutics: Prophylactic Options to Environmental and Contagious Threats (ADEPT-PROTECT).[11] Its stated goal was to develop an mRNA vaccine with the capability to suppress a global pandemic within 60 days. In January 2014, the company entered an agreement with Alexion Pharmaceuticals to develop treatments against ten diseases.[12] On January 14, 2014, Moderna announced the creation of its first venture, Onkaido Therapeutics, to focus "exclusively on developing mRNA-based oncology treatments."[13][14] It launched its second venture, Valera, in January 2015, with a focus on "viral, bacterial and parasitic infectious diseases."[15][16] Employees of Valera and Moderna developed an mRNA vaccine candidate against Zika virus infection.[17] Another venture, Elpidera, was announced in May 2015 to continue work on RNA therapies advancing Moderna's work with Alexion.[18][19]

In 2015, the company formed a partnership with Merck & Co. to develop treatments for cancer, and in 2016 the company formed a partnership with Vertex Pharmaceuticals to develop treatments for cystic fibrosis.[10][20][21][22] In January 2016, the Bill & Melinda Gates Foundation committed to provide at least $20 million in grant funding to the company.[1] In 2017, Alexion terminated its partnership with Moderna after safety issues prevented their work from reaching human trials.[23]

ADEPT : PROTECT

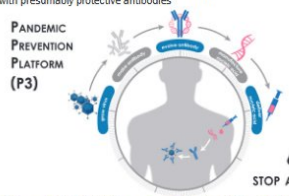
THE NEED AND OPPORTUNITY

A primary objective of DARPA's Biological Technologies Office (BTO) is to better ensure the health, and thereby the force readiness, of the country's military service community. The COVID-19 pandemic, which rapidly spread worldwide from an initial outbreak in China at the end of 2019, highlights one of the most perilous vulnerabilities to deployed military personnel and civilians: lack of protection and medical countermeasures (MCMs) against endemic and emerging biothreats. The Zika outbreak in 2015-2016, the more recent Ebola outbreak in the Democratic Republic of Congo, and mosquito-borne viruses such as Chikungunya and Dengue are among these threats.

Vaccines are the traditional mainstay of long-term infection prevention, while antibody approaches have at times been used to treat active infections. In one antibody-based approach that is being applied on a small scale in the current pandemic, blood serum with presumably protective antibodies obtained from those who have recovered from an infection is infused into patients. In more recent decades, monoclonal antibodies manufactured in cultured immune-system cells have been used to treat certain cancers and immune disorders. However, these treatments have suffered from shortcomings – including slow development, expensive manufacture, and dependence on continuous cold storage – that have prevented widespread use by the military.

THE DARPA SOLUTION

In 2012 with the ADEPT:PROTECT program*, DARPA began investing in the development of gene-encoded vaccines, a new category of preventive measures based on DNA or RNA. In this approach, genes that encode immune-stimulating antigens, such as the spike proteins on the surfaces of viruses like the one (SARS-CoV-2) that causes COVID-19, are delivered directly to a recipient's body. There, the instructions carried in the DNA or RNA elicit the body's own cells to manufacture the antigenic viral protein, which, in turn, elicits an immune response to the virus.



A follow-on effort to the ADEPT program, known as the Pandemic Prevention Platform program, aims to take pandemics off of the list of humanity's angsts with a range of technologies and practices marked by early detection of an outbreak and, within 60 days, development and widescale deployment of protective countermeasures.

Gene-based vaccines have shown great promise as a means to provide safe, reproducible, long-term immune protection. For vaccines to work, however, they often require more than one dose and it often takes weeks to months before a recipient's immune system builds up sufficient protection again the vaccine's viral target. With these biomedical realities come threats to warfighters if they deploy to pathogen-rife regions before having established relevant immunity and threats to military missions due to delayed deployment of personnel until they achieve immune protection.

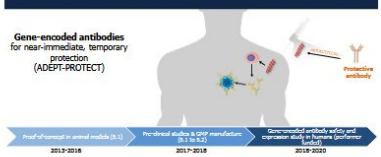
For a vaccine to confer immunity, it must lead to the production within a recipient of highly potent antibodies that can neutralize the pathogen. DARPA initiated the ADEPT:PROTECT program (most often referred to more simply as ADEPT) with the intention of bushwhacking a novel pathway to near-immediate protection against pathogens for which vaccines are not yet available and to confer interim-term protection during the development of a vaccine, which can take years.

THE IMPACT

DARPA's investments in this space led directly, with the biotechnology firm Moderna as a contracted performer on the program, to a first-ever human clinical trial with an RNA vaccine in 2019.

Earlier proof-of-concept experiments funded under ADEPT primarily with 6.1 funding (for basic research) demonstrated that delivery of antibody-making instructions – by way of messenger ribonucleic acid (mRNA), deoxyribonucleic acid (DNA), or another genetic-information-carrying tactic that relies on small viruses known as adenovirus-associated viruses (AAVs) – led to the production of antibodies that conferred protection in test animals exposed to the mosquito-borne Chikungunya (ChikV) virus.

DARPA pioneered the use of the body as a bioreactor to produce prophylactic antibodies to protect against biothreats



In a more applied phase of technology development, Moderna was converted to 6.2 funding (applied research) to begin pre-clinical studies in non-human primates with an RNA-encoded antibody against ChikV and to produce the countermeasure using Good Manufacturing Practices (GMP), which regulatory agencies such as the Food and Drug Administration often require.

Moderna subsequently used company funding to conduct a Phase I clinical trial with 22 healthy volunteers using an mRNA-encoded ChikV antibody. This marked the first safety demonstration of an RNA-based medical countermeasure. Moderna reported these promising results of its clinical study in 2019. The trial demonstrated platform safety as well as the ability to generate protective levels of functional antibody in humans. In response to COVID-19, Moderna in March 2020 initiated human trials of gene-encoded antibodies that target SARS-CoV-2.

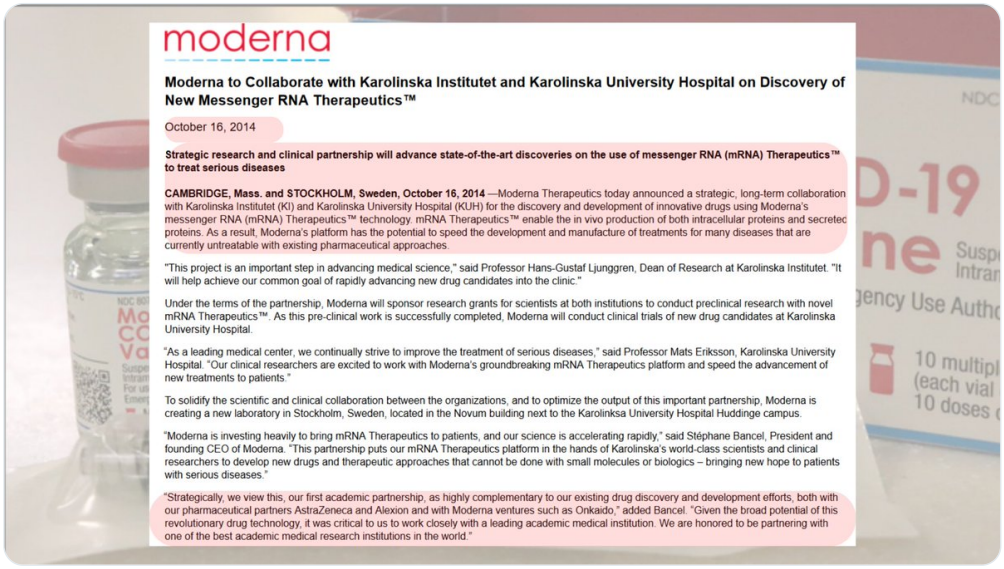
Research by Moderna and other ADEPT performers has provided proof-of-concept results that simultaneously delivering gene-encoded antibody treatment and vaccine confers the recipient with immediate immune protection while a long-term immune response develops.

LOOKING AHEAD

DARPA's R&D investments to de-risk the pathway to gene-based medical countermeasures have spurred like-minded innovators. In addition to Moderna, several other companies, including AstraZeneca and Inovio, have made major investments in this budding biomedical field. These DARPA investments also spurred the biotech firm RenBio to work toward optimizing the delivery of gene-based MCMs for increased efficacy and tolerability. Other government agencies – including the DoD's Joint Program Executive Office for Chemical, Biologic, Radiological, and Nuclear Defense (JPEO-CBRND), the Biomedical Advanced Research and Development Authority (BARDA), and the National Institute of Allergy and Infectious Disease (NIAID) – also have recognized the power of gene-encoded antibody technology to fight a range of biothreats and infectious diseases.

Progress in the ADEPT program has earned supplemental 6.2 funding from the U. S. Congress in response to the 2014 Ebola virus outbreak in West Africa. To address current and future Ebola outbreaks, these funds were directed toward development, manufacture, and/or clinical evaluation of several MCMs, including one

4🧵 One year later in 2014, Moderna lands a collaboration with the Karolinska Institute [KI] in Sweden. Important to note that one of their founders, Ken Chien was a research director at KI since 2013, his specialty was cardiovascular biotechnology. Just before Chien started at KI, he was approached by another Moderna Founder, Derrick Rossi to begin creating what would become Moderna. Chein's focus after that was focused on his studies that found "mRNA in heart muscle, resulting in a patent on the discovery that triggered mRNA towards therapeutic applications."


moderna

Moderna to Collaborate with Karolinska Institutet and Karolinska University Hospital on Discovery of New Messenger RNA Therapeutics™

October 16, 2014

Strategic research and clinical partnership will advance state-of-the-art discoveries on the use of messenger RNA (mRNA) Therapeutics™ to treat serious diseases

CAMBRIDGE, Mass. and STOCKHOLM, Sweden, October 16, 2014 —Moderna Therapeutics today announced a strategic, long-term collaboration with Karolinska Institutet (KI) and Karolinska University Hospital (KUH) for the discovery and development of innovative drugs using Moderna's messenger RNA (mRNA) Therapeutics™ technology. mRNA Therapeutics™ enable the in vivo production of both intracellular proteins and secreted proteins. As a result, Moderna's platform has the potential to speed the development and manufacture of treatments for many diseases that are currently untreatable with existing pharmaceutical approaches.

"This project is an important step in advancing medical science," said Professor Hans-Gustaf Ljunggren, Dean of Research at Karolinska Institutet. "It will help achieve our common goal of rapidly advancing new drug candidates into the clinic."

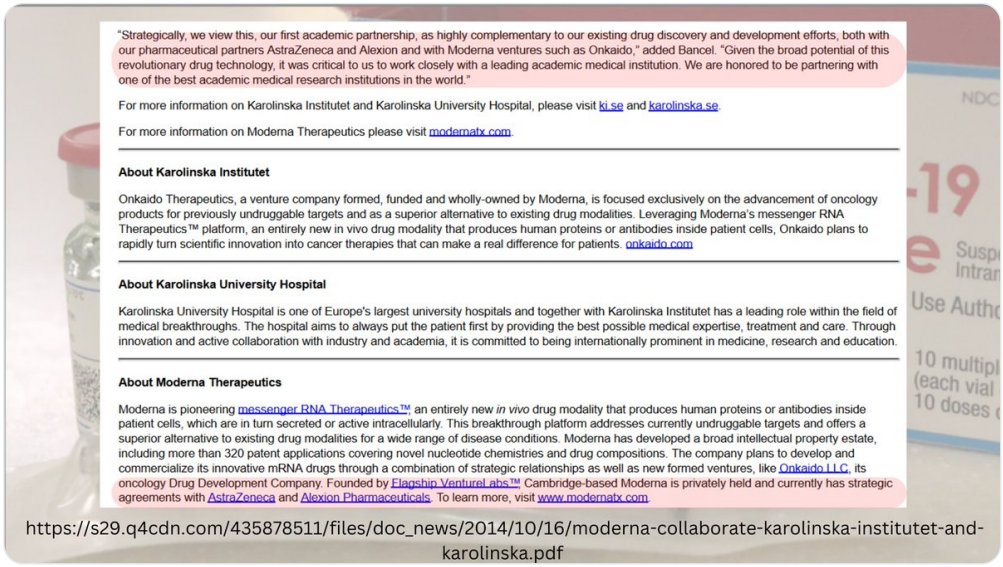
Under the terms of the partnership, Moderna will sponsor research grants for scientists at both institutions to conduct preclinical research with novel mRNA Therapeutics™. As this pre-clinical work is successfully completed, Moderna will conduct clinical trials of new drug candidates at Karolinska University Hospital.

"As a leading medical center, we continually strive to improve the treatment of serious diseases," said Professor Mats Eriksson, Karolinska University Hospital. "Our clinical researchers are excited to work with Moderna's groundbreaking mRNA Therapeutics platform and speed the advancement of new treatments to patients."

To solidify the scientific and clinical collaboration between the organizations, and to optimize the output of this important partnership, Moderna is creating a new laboratory in Stockholm, Sweden, located in the Novum building next to the Karolinksa University Hospital Huddinge campus.

"Moderna is investing heavily to bring mRNA Therapeutics to patients, and our science is accelerating rapidly," said Stéphane Bancel, President and founding CEO of Moderna. "This partnership puts our mRNA Therapeutics platform in the hands of Karolinska's world-class scientists and clinical researchers to develop new drugs and therapeutic approaches that cannot be done with small molecules or biologics – bringing new hope to patients with serious diseases."

"Strategically, we view this, our first academic partnership, as highly complementary to our existing drug discovery and development efforts, both with our pharmaceutical partners AstraZeneca and Alexion and with Moderna ventures such as Onkaido," added Bancel. "Given the broad potential of this revolutionary drug technology, it was critical to us to work closely with a leading academic medical institution. We are honored to be partnering with one of the best academic medical research institutions in the world."



"Strategically, we view this, our first academic partnership, as highly complementary to our existing drug discovery and development efforts, both with our pharmaceutical partners AstraZeneca and Alexion and with Moderna ventures such as Onkaido," added Bancel. "Given the broad potential of this revolutionary drug technology, it was critical to us to work closely with a leading academic medical institution. We are honored to be partnering with one of the best academic medical research institutions in the world."

For more information on Karolinska Institutet and Karolinska University Hospital, please visit ki.se and karolinska.se.

For more information on Moderna Therapeutics please visit modernatx.com.

About Karolinska Institutet

Onkaido Therapeutics, a venture company formed, funded and wholly-owned by Moderna, is focused exclusively on the advancement of oncology products for previously undruggable targets and as a superior alternative to existing drug modalities. Leveraging Moderna's messenger RNA Therapeutics™ platform, an entirely new in vivo drug modality that produces human proteins or antibodies inside patient cells, Onkaido plans to rapidly turn scientific innovation into cancer therapies that can make a real difference for patients. onkaido.com

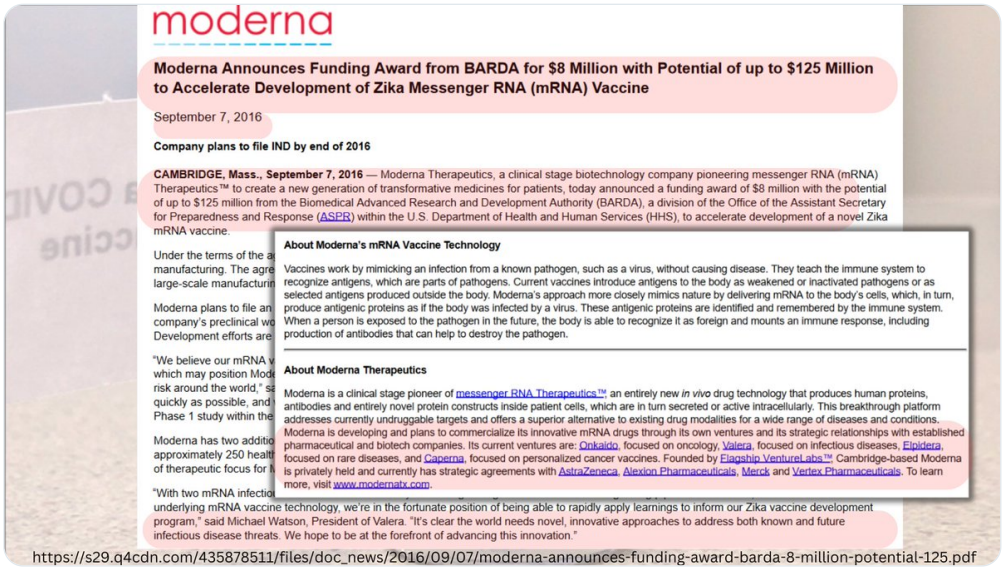
About Karolinska University Hospital

Karolinska University Hospital is one of Europe's largest university hospitals and together with Karolinska Institutet has a leading role within the field of medical breakthroughs. The hospital aims to always put the patient first by providing the best possible medical expertise, treatment and care. Through innovation and active collaboration with industry and academia, it is committed to being internationally prominent in medicine, research and education.

About Moderna Therapeutics

Moderna is pioneering messenger RNA Therapeutics™ an entirely new *in vivo* drug modality that produces human proteins or antibodies inside patient cells, which are in turn secreted or active intracellularly. This breakthrough platform addresses currently undruggable targets and offers a superior alternative to existing drug modalities for a wide range of disease conditions. Moderna has developed a broad intellectual property estate, including more than 320 patent applications covering novel nucleotide chemistries and drug compositions. The company plans to develop and commercialize its innovative mRNA drugs through a combination of strategic relationships as well as new formed ventures, like Onkaido LLC, its oncology Drug Development Company. Founded by Flagship VentureLabs™ Cambridge-based Moderna is privately held and currently has strategic agreements with AstraZeneca and Alexion Pharmaceuticals. To learn more, visit www.modernatx.com.

https://s29.q4cdn.com/435878511/files/doc_news/2014/10/16/moderna-collaborate-karolinska-institutet-and-karolinska.pdf



moderna

Moderna Announces Funding Award from BARDA for $8 Million with Potential of up to $125 Million to Accelerate Development of Zika Messenger RNA (mRNA) Vaccine

September 7, 2016

Company plans to file IND by end of 2016

CAMBRIDGE, Mass., September 7, 2016 — Moderna Therapeutics, a clinical stage biotechnology company pioneering messenger RNA (mRNA) Therapeutics™ to create a new generation of transformative medicines for patients, today announced a funding award of $8 million with the potential of up to $125 million from the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS), to accelerate development of a novel Zika mRNA vaccine.

Under the terms of the a
manufacturing. The agre
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Moderna plans to file an
company's preclinical wo
Development efforts are

"We believe our mRNA v
which may position Mod
risk around the world," s
quickly as possible, and
Phase 1 study within the

Moderna has two additio
approximately 250 healt
of therapeutic focus for h

"With two mRNA infectio
underlying mRNA vaccine technology, we're in the fortunate position of being able to rapidly apply learnings to inform our Zika vaccine development program," said Michael Watson, President of Valera. "It's clear the world needs novel, innovative approaches to address both known and future infectious disease threats. We hope to be at the forefront of advancing this innovation."

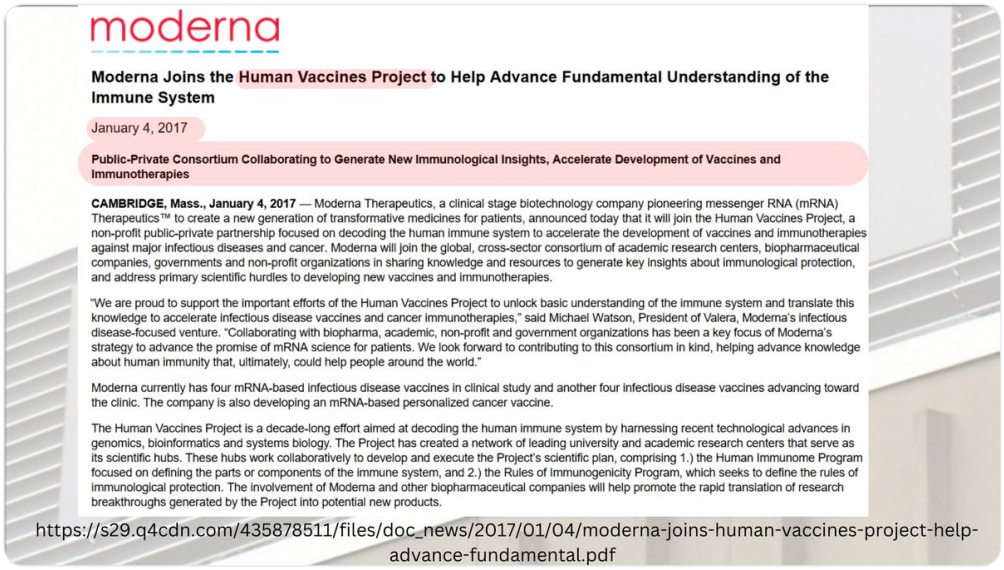
About Moderna's mRNA Vaccine Technology

Vaccines work by mimicking an infection from a known pathogen, such as a virus, without causing disease. They teach the immune system to recognize antigens, which are parts of pathogens. Current vaccines introduce antigens to the body as weakened or inactivated pathogens or as selected antigens produced outside the body. Moderna's approach more closely mimics nature by delivering mRNA to the body's cells, which, in turn, produce antigenic proteins as if the body was infected by a virus. These antigenic proteins are identified and remembered by the immune system. When a person is exposed to the pathogen in the future, the body is able to recognize it as foreign and mounts an immune response, including production of antibodies that can help to destroy the pathogen.

About Moderna Therapeutics

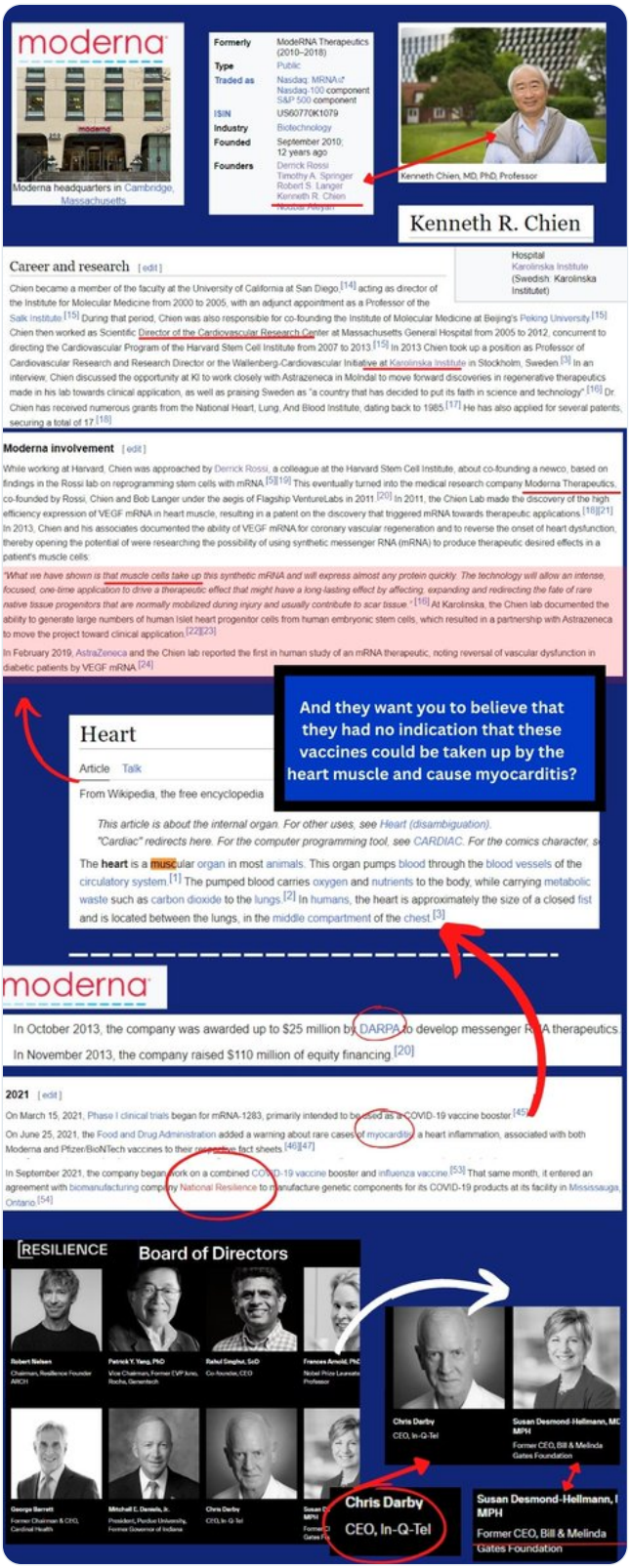
Moderna is a clinical stage pioneer of messenger RNA Therapeutics™ an entirely new *in vivo* drug technology that produces human proteins, antibodies and entirely novel protein constructs inside patient cells, which are in turn secreted or active intracellularly. This breakthrough platform addresses currently undruggable targets and offers a superior alternative to existing drug modalities for a wide range of diseases and conditions. Moderna is developing and plans to commercialize its innovative mRNA drugs through its own ventures and its strategic relationships with established pharmaceutical and biotech companies. Its current ventures are: Onkaido, focused on oncology, Valera, focused on infectious diseases, Elpidera, focused on rare diseases, and Caperna, focused on personalized cancer vaccines. Founded by Flagship VentureLabs™ Cambridge-based Moderna is privately held and currently has strategic agreements with AstraZeneca, Alexion Pharmaceuticals, Merck and Vertex Pharmaceuticals. To learn more, visit www.modernatx.com.

https://s29.q4cdn.com/435878511/files/doc_news/2016/09/07/moderna-announces-funding-award-barda-8-million-potential-125.pdf



https://s29.q4cdn.com/435878511/files/doc_news/2017/01/04/moderna-joins-human-vaccines-project-help-advance-fundamental.pdf

5🧵 Almost 2yrs ago I made this infographic to highlight these details. *As a side note; #BillGates the eugenics-minded college drop-out that pretends he's a doctor actually got a degree, albeit honorary, from the Karolinska Institute in 2004. https://www.fiercebiotech.com/biotech/press-release-bill-and-melinda-gates-to-receive-honorary-degrees-from-karolinska-institutet



6🧵 Where things get strange is when you find o/that BEFORE Baric started playing Frankenstein w/ Bat CoVs he was messing with Rabbit CoVs. In his 1992 publication Baric explored how Rabbit's infected w/CoVs suffered Myocarditis. Oddly its a similar mechanism to what Chien was looking into at KI when he started Moderna.

Pfizer

Science Products Stories Newsroom About

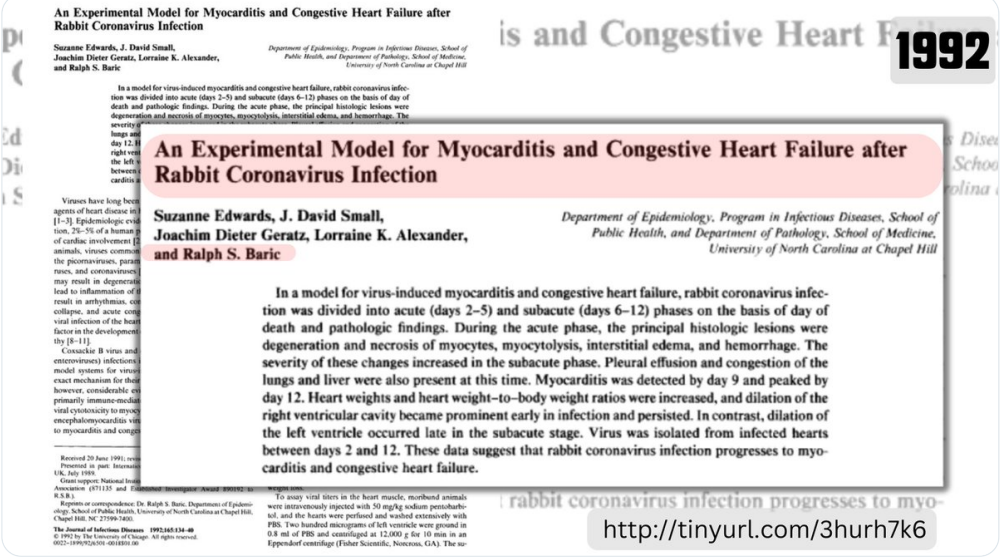
Pfizer Press release | Covid-19 | Vaccines

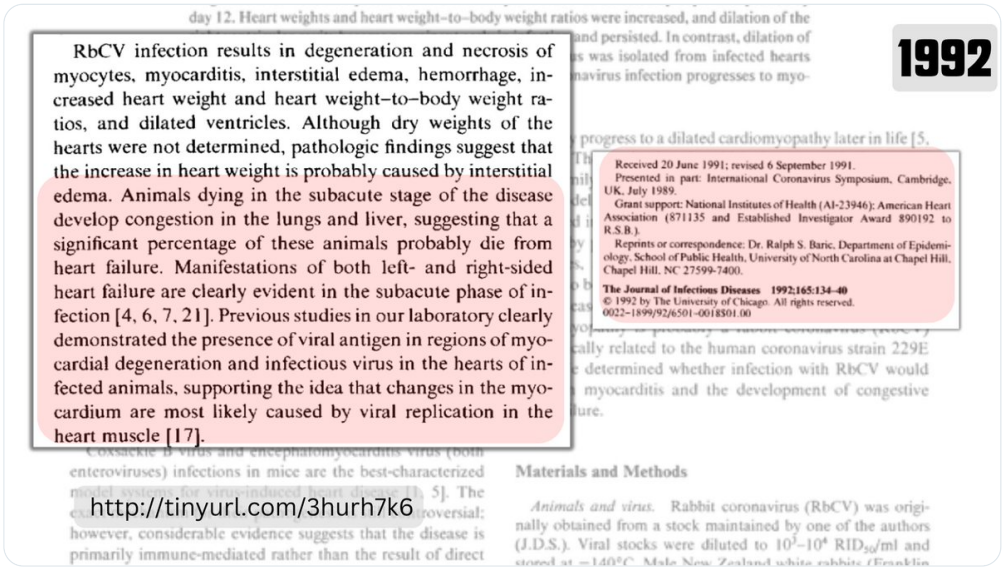
Pfizer and BioNTech Receive Expanded U.S. FDA Emergency Use Authorization of COVID-19 Vaccine Booster to Include Individuals 18 and Older

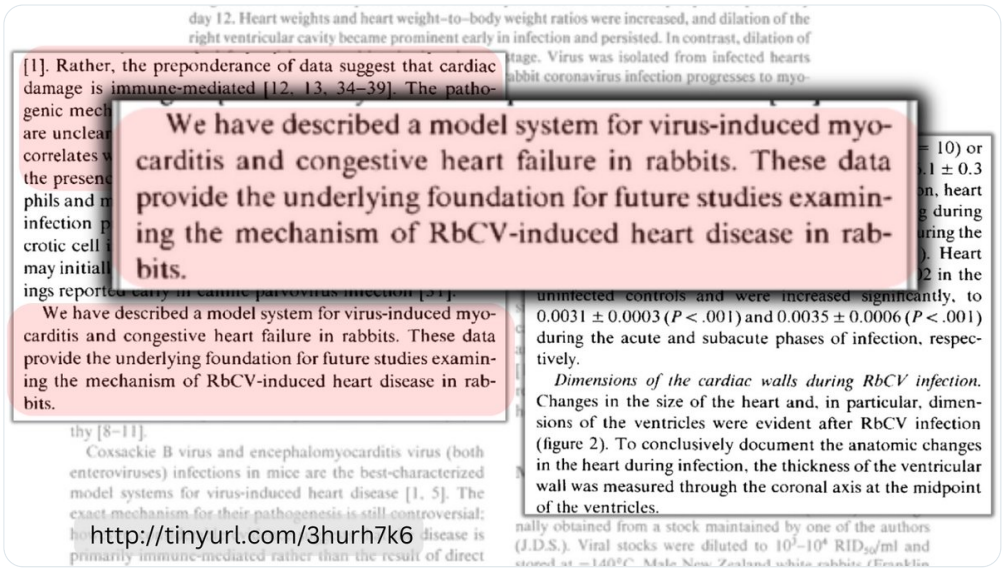
Friday, November 19, 2021 - 08:25am

- *Expanded authorization allows more Americans to receive a booster dose to help preserve a high-level of protection against COVID-19*

NEW YORK & MAINZ, Germany--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) and BioNTech SE (Nasdaq: BNTX) today announced that the U.S. Food and Drug Administration (FDA) has expanded the emergency use authorization (EUA) of a booster dose of the Pfizer-BioNTech COVID-19 Vaccine to include individuals 18 years of age and older. The booster dose is to be







7🧵 We now know that Pfizer, who stole the mRNA C19 formula from Moderna, had known that Myocarditis was a Serious Adverse Event for their injections LONG before it was made public in November 2021 after it had been injected into billions of people. This has since been admitted by Pfizer & covered by great minds like @P_McCulloughMD & @JesslovesMJK

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10823859/

ECHOCARDIOGRAPHIC CHANGES FOLLOWING RABBIT CORONAVIRUS INFECTION

Lorraine K. Alexander, Bruce W. Keene, and Ralph S. Baric

The Department of Epidemiology
The University of North Carolina at Chapel Hill
Chapel Hill, North Carolina
The College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina

Much of our understanding of the mechanisms by which viruses cause myocarditis and/or dilated cardiomyopathy (DCM) is based on animal models of virus-induced heart disease. Information concerning cardiac function during acute and/or chronic viral infection in these models is limited (1). A well defined model in a species conducive to monitoring of cardiac function is needed to enhance our understanding of viral induced heart disease. We have previously demonstrated that rabbit coronavirus (RbCV) infection results in degeneration and necrosis of myocytes, myocarditis, and gross organ and histopathologic changes of DCM (2,3). We have also shown that electrocardiographic changes observed during RbCV infection mimic those in humans with myocarditis and DCM (submitted). This chapter describes the echocardiographic changes observed during RbCV infection.

Eleven male New Zealand white rabbits were sedated prior to echocardiography with a combination of xylazine (0.17 mg/kg) and ketamine (17 mg/kg). An electrocardiogram was monitored continuously during echocardiography and two-dimensional echocardiographic views were recorded with the animal in right lateral recumbancy from the right parasternal long and short-axis positions using a 7.5 MHz annular array transducer. Measurements of left ventricular (LV) size, systolic function, mitral valve motion, and aortic and left atrial diameter were made according to the American Society of Echocardiography standards for M-mode echocardiography. Briefly, M-mode measurements included LV end diastolic and systolic chamber dimensions and wall thickness obtained by guiding the M-mode cursor between the papillary muscles from a right parasternal short-axis imaging plane just ventral to the mitral valve leaflets at the level of the chordae tendinae. Aortic and left atrial dimensions were measured from an M-mode view obtained by guiding the cursor through the aorta and left atrium in a right parasternal short short axis view at the level of the aortic valve. The mitral valve motion and E-point - septal separation was observed and recorded from M-mode images obtained by guiding the cursor through a right parasternal

Corona- and Related Viruses, Edited by P. J. Talbot and G. A. Levy

Table 1. Cardiac function values for 11 RbCV infected rabbits

Measurement	Uninfected[a] n = 11	Nonsurvivor[a,b] n= 6	Survivor[a,b] n= 5
Left Ventricular (LV) diameter (d)[c] (cm)	1.42 ± 0.24	1.13 ± 0.44	1.14 ± 0.12
LV diameter (s)[d] (cm)	0.92 ± 0.17	0.93 ± 0.38	0.84 ± 0.17
% fractional shortening	35.5 ± 4.85	17.33 ± 6.19	26.17 ± 12
Septal wall thickness (d) (cm)	0.22 ± 0.07	0.25 ± 0.06	0.22 ± 0.05
Septal wall thickness (s) (cm)	0.38 ± 0.08	0.28 ± 0.09	0.33 ± 0.12
LV posterior wall thickness (d) (cm)	0.31 ± 0.11	0.32 ± 0.08	0.26 ± 0.03
LV posterior wall thickness (s) (cm)	0.50 ± 0.12	0.44 ± 0.13	0.42 ± 0.06
Left atrium diamter (cm)	0.88 ± 0.14	0.93 ± 0.15	0.86 ± 0.10
Aorta (cm)	0.66 ± 0.12	0.74 ± 0.13	0.68 ± 0.05
Left atrium/Ao	1.22 ± 0.20	1.36 ± 0.29	1.28 ± 0.14
E-point septal separation (EPSS)	0.14 ± 0.04	0.22 ± 0.16	0.126± 0.09

a = Mean ± SD.
b = Day 3 after infection.
c = diastole.
d = systole.

short axis view at the level of the mitral valve. LV fractional shortening was calculated as an ejection phase index of systolic function. All values reported reflect the mean of 3 measurements made on sinus beats. Rabbits were infected with 0.3 ml of a 1X 10^3 - 1X 10^4 RID_{50} of RbCV and echocardiographic measurements were repeated using the same anesthetic and measurement protocol on days 3, 6, 9, 12 and 30 post-infection.

Two (18%) rabbits died during the acute phase of infection (day 3), 4 (36%) died in the early subacute phase (day 6), and 5 (46%) survived beyond day 12 into the chronic phase. Echocardiographic data is displayed in Table 1. The index of systolic ventricular function

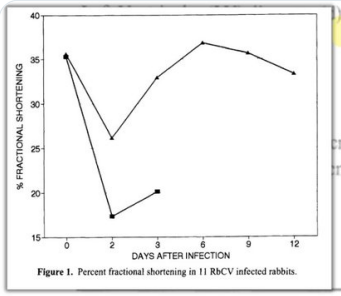
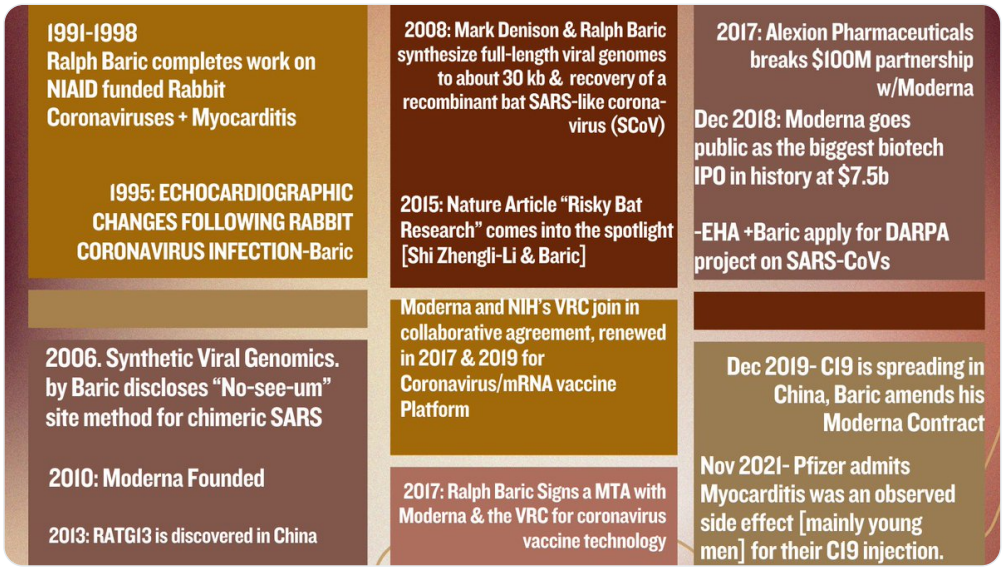


Figure 1. Percent fractional shortening in 11 RbCV infected rabbits.

chosen, % fractional shortening was depressed in all infected rabbits by day 3 post infection (Figure 1). Fractional shortening was more depressed in nonsurvivors (17.33 ± 6.19%, p= <.001 from controls) as compared to survivors (26.17 ± 12%, ns from control). Mean LV wall thickness, chamber dimensions, and left atrial dimensions were not significantly different from controls throughout the study in either survivors or nonsurvivors. These findings confirm our previous pathologic studies in which rabbits dying early in infection (days 2-5) did not have significantly different LV wall thickness, and chamber dimensions from control animals.

We conclude that RbCV infection depresses an ejection phase index of systolic LV function, that this depression precedes gross morphologic changes in the ventricle, and that severe systolic dysfunction correlates positively with mortality. These findings provide a direct link between the severity of virus-induced cardiac dysfunction and survival during RbCV infection, characterizing a reproducible model of cardiac dysfunction following viral infection of the heart.



8🧵This thread is already not for the faint of heart, so to save time I suggest reading the details of the MTA between Moderna, Baric and the NIH's VRC leading up to 2020: & how Moderna made the C19 jab formulation in ONE DAY:

Destiny Rezendes
@dezzie_rezzie · **Follow**

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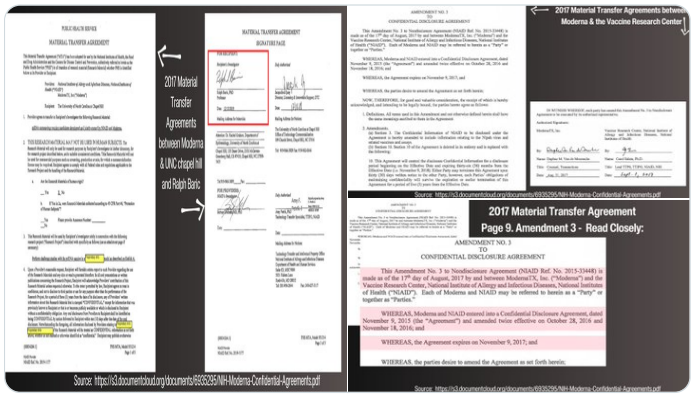
8🧵In that same MTA, later amended, Ralph Baric signs the MTA in 2019 for the same technology but read Amendment 3 carefully. According to the contract, the collaboration between VRC and Moderna didn't start in 2017, but rather on Nov 9, 2015.🔎🤫



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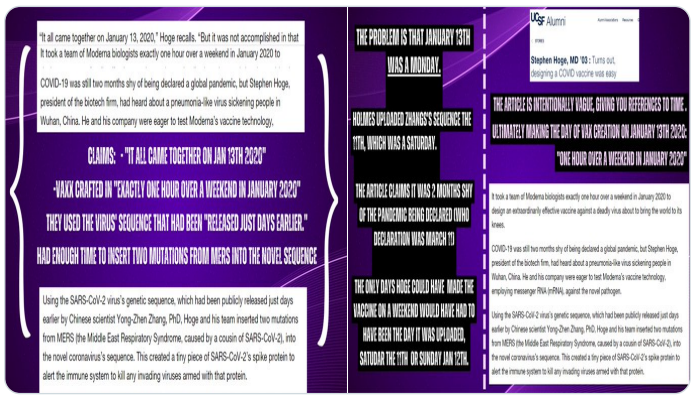
10🧵Hoge (Moderna) claims he created the C19 💉in 1hr, over a weekend on Jan 13th 2020. However, the 13th was a weekday- a Monday. Zhang/Howell uploaded the sequence on Sat. the 11th. Hoge admits he was "Eager" to get to "Test" out the 💉.



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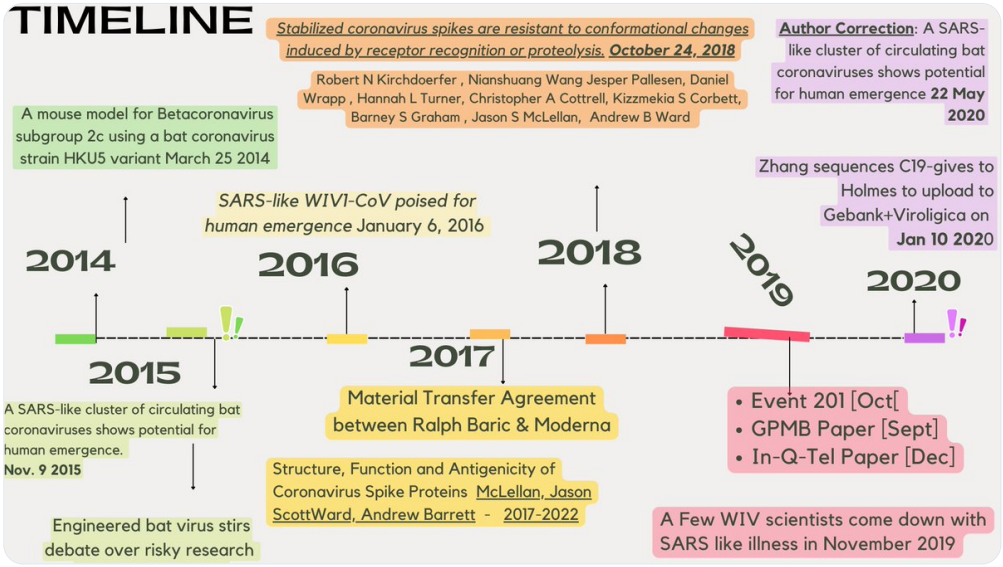

JOURNAL ARTICLE

An Experimental Model for Myocarditis and Congestive Heart Failure after Rabbit Coronavirus Infection

Suzanne Edwards, J. David Small, Joachim Dieter Geratz, Lorraine K. Alexander and Ralph S. Baric

The Journal of Infectious Diseases

Vol. 165, No. 1 (Jan., 1992), pp. 134-140 (7 pages)

Published By: Oxford University Press

About the Human Vaccines Project

The Human Vaccines Project is a non-profit public-private partnership with the mission to accelerate the development of vaccines and immunotherapies against major infectious diseases and cancers by decoding the human immune system. The Project has a growing list of partners and financial supporters including: Vanderbilt University Medical Center, the J. Craig Venter Institute, the La Jolla Institute, The Scripps Research Institute, UC San Diego, Aeras, Boehringer Ingelheim, Crucell/Janssen, GSK, Pfizer, MedImmune, Regeneron, Sanofi Pasteur, the Robert Wood Johnson Foundation and the John D. and Catherine T. MacArthur Foundation. The Project brings together leading academic research centers, industrial partners, nonprofits and governments to address the primary scientific barriers to developing new vaccines and immunotherapies, and has been endorsed by 35 of the world's leading vaccine scientists. www.humanvaccinesproject.org

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About Moderna Therapeutics

Moderna is a clinical stage pioneer of messenger RNA Therapeutics™; an entirely new in vivo drug technology that directs the body's cells to produces human proteins, antibodies and entirely novel protein constructs, which are in turn secreted or active intracellularly. With its breakthrough platform, Moderna is developing mRNA vaccines and therapeutics to address currently undruggable targets and deliver a new class of medicines for a wide range of diseases and conditions. Moderna is developing and plans to commercialize its innovative mRNA medicines for infectious diseases, cancer (immunooncology), rare diseases, cardiovascular disease and pulmonary disease, through its ecosystem of internal ventures and strategic partners.

Headquartered in Cambridge, Mass., privately held Moderna currently has strategic agreements with AstraZeneca, Merck, Alexion Pharmaceuticals and Vertex Pharmaceuticals, as well as the Defense Advanced Research Projects Agency (DARPA), an agency of the U.S. Department of Defense; the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS); and the Bill & Melinda Gates Foundation. To learn more, visit www.modernatx.com.

Moderna Contacts:

Investors:
Maren Winnick
617-674-5297

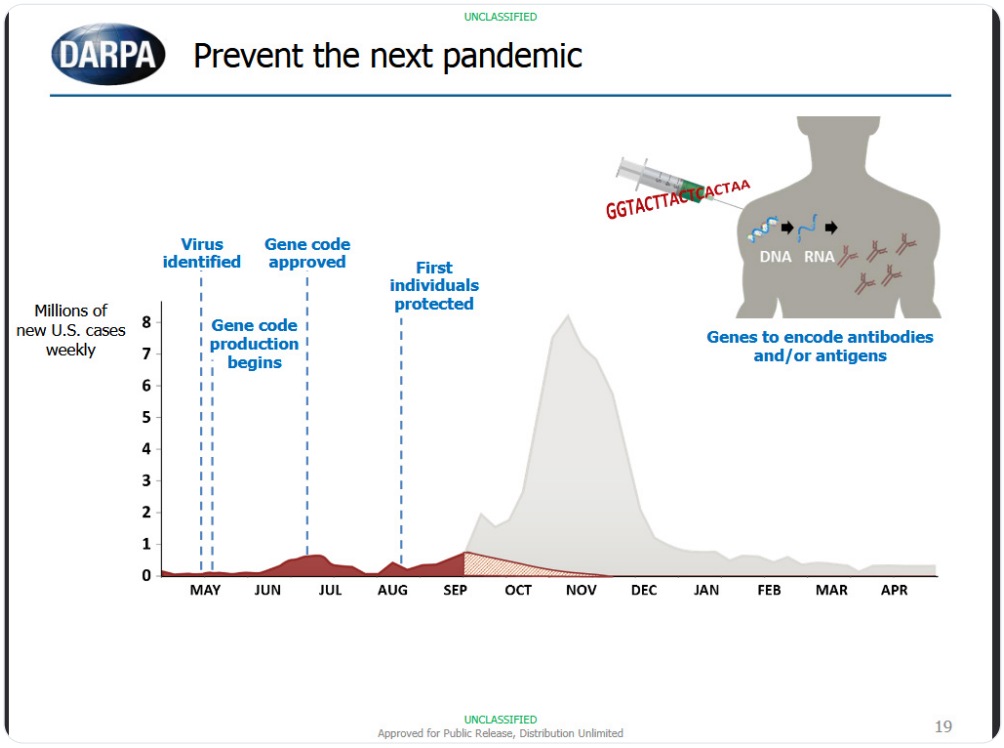
9🧵What's the tie? DARPA's wishes of Synthetic Biology and Rapid Countermeasure deployments who outside of the DEFUSE project was ALREADY working with Moderna who was ALREADY working with Ralph Baric before the pandemic started! You'll see this truth in DARPA's internal document [unclassified] from 2017👇

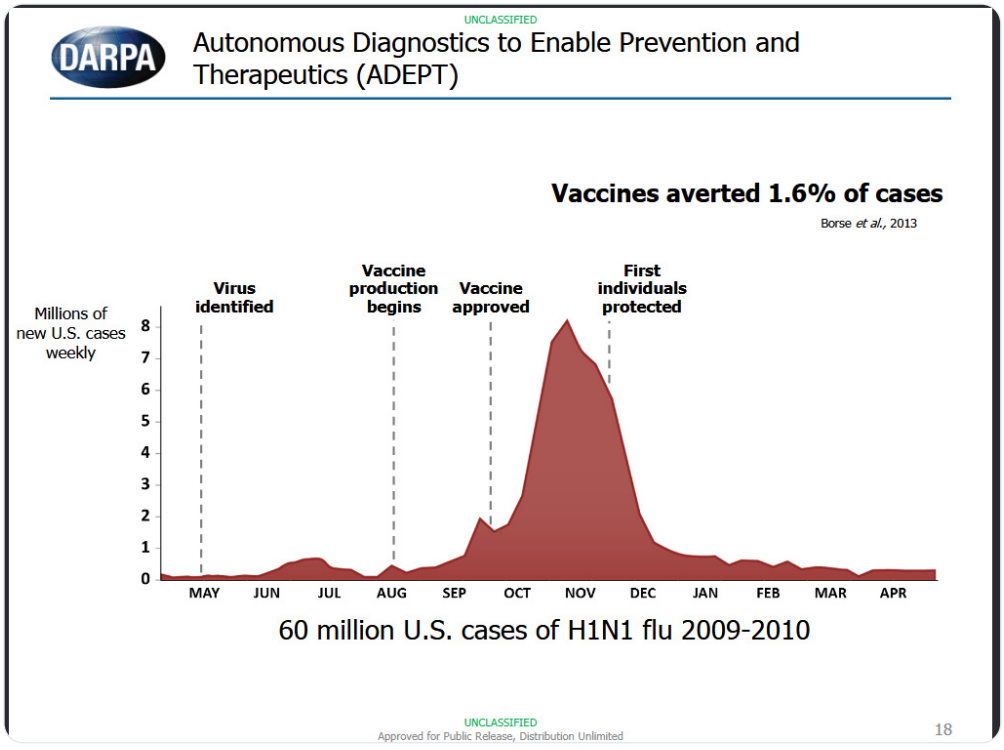
Defense Advanced Research Projects Agency

Stefanie Tompkins, Ph.D.
Acting Deputy Director

NDIA S&ET Conference

April 18, 2017





10🧵 The reality is DARPA didn't approve the DEFUSE project likely because they realized they didn't need EHA to move forward w/their goals. Eco Health was already deep in w/ USAID [CIA front] & according to Chris Darby of In-Q-Tel in 2019, the intelligence community's top focus was bio-data.

-Eco Health was successful in its role with USAID in China and SE Asia & ADEPT was already making great strides, as was Moderna & Baric.

-So, Baric knew since the 1990's that CoV's could cause Myocarditis in infected mammals that was similar to its presentation in humans.

-The scientific community knew since 2003/4 that SARS vaccines were largely ineffective and that the spike protein and mRNA bio-accumulated in vital organs, like the heart.

-The US's biological research oversight group, the NSABB, knew since 2006/7 that Baric could create a full CoV genome WITHOUT leaving a trace that it was lab altered & NIH knew [because they funded it] that Baric was doing GOF research with Corona-Virologists in Wuhan and w/ EHA.

-The USG KNEW since 2018/2019 that Wuhan Institute of Virology was lacking in their safety regulations [despite being trained by University of TX Medical Branch staff] and they knew the science was ongoing regardless.

-HHS knew that Baric led the forefront on not only the vaccine [Moderna] but also the heavily pushed his Monoclonal antibody "treatment" Remdesivir, which is a FAILED Hept/Ebola/Zika "treatment" and the men who helped him; Mark Denison & Barney Graham all received MILLIONS after the "vaccine rollout" allotted to their establishments for intellectual property rights [Vanderbilt Univ, Vaccine Research Center/NIH]

AND YET... The Peter Daszak Transcript from NOV 2023 has not been released! The recent Fauci transcript has YET TO BE RELEASED. AND RALPH BARIC HAS NEVER HAD TO BE HELD ACCOUNTABLE or properly investigated over C19!

The USG put 5 TRILLION DOLLARS into a "Pandemic Oversight Fund" [the largest financial effort in mankind's history] but they can't afford to investigate this pandemic or vaccine which has Injured and killed people all over the world.

What about those who lost their kids to Myocarditis post vaccination?! You're gonna tell them its all a coincidence and it was "for the greater good?"

Despite what CCN medical correspondent, & freedom-hater, Dr. Leana Wen thinks, WE ARE NOT RABBITS. We are humans who deserve the truth & I shouldn't have to throw my life away to learn all this crap!

I'm not apologizing for the long post- You don't like it then do it yourself. Otherwise, links will be added [if not already on the slides] as a comment to avoid algorithm throttling.

SOURCES

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More Links:
Gates Karolinska 2014:

Pubmed Myocarditis Eval 2022:

DARPA 2017/ADEPT program Unclassified:

Moderna on mRNA +DARPA from 2018 Internal Doc pg 27-57:

Moderna's beginnings 2017 article:

ADEPT-Protect:

Jessica Rose & @P_McCulloughMD 's Jan 2024 paper on Vaccine induced Myocarditis 🔥:

1995 Baric article:ECHOCARDIOGRAPHIC CHANGES
FOLLOWING RABBIT CORONAVIRUS INFECTION

Baric article on CoV induced Myocarditis in Rabbits:

Archive of Pfizer's release statement on Myocarditis:

All other used references are in the Sources Image at the end of the thread. Thank you and God Blesshttps://www.fiercebiotech.com/biotech/press-release-bill-and-melinda-gates-to-receive-honorary-degrees-from-karolinska-institutet
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Key partner cuts ties with brash biotech startup Moderna, raising big ...
Moderna Therapeutics, a $5 billion startup that boasts of changing the world, is losing a key partner, imperiling its most advanced drug project.
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